Nivolumab

An HCP Tool From AIM with Immunotherapy

Nivolumab (Opdivo®) is an anti-programmed death receptor-1 (PD-1) monoclonal antibody that binds to PD-1, a checkpoint control. PD-1 is a negative regulator of T-cell activation and proliferation, meaning PD-1 engagement will turn the immune response off, essentially acting as a brake to an immune reaction. For this reason, PD-1 and other regulators acting in this manner are known as immune checkpoints.

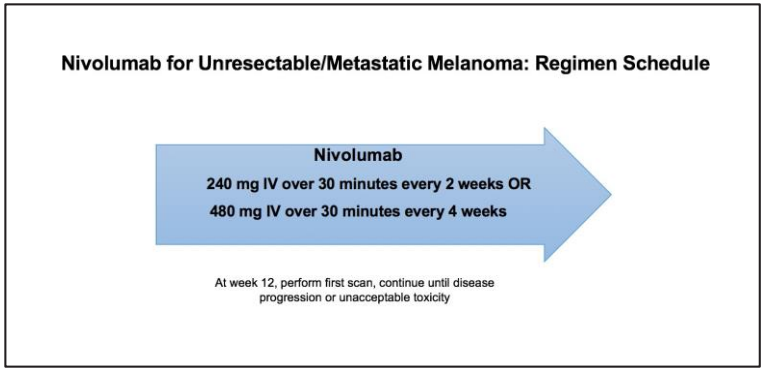
This type of inhibitory role is necessary for a normal system to prevent an excessive immune reaction and potentially lethal autoimmune response. Unfortunately, some tumors can exploit the PD-1 pathway, enabling them to evade an immune response by engaging the shut-off actions of PD-1. Nivolumab selectively binds to PD-1, thus physically blocking the engagement of PD-1 and preventing the immune system from being shut off by tumor cells. This allows the immune response to recognize the tumor cells and take action.

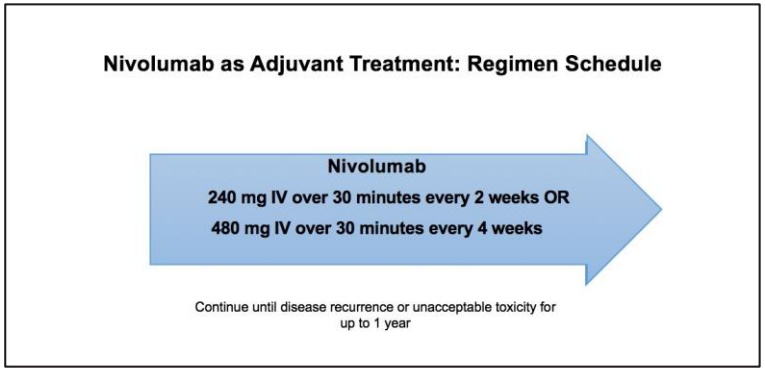
Nivolumab is indicated as treatment for various cancer types including classic Hodgkin lymphoma, colorectal cancer, esophageal adenocarcinoma, gastric cancer, gastroesophageal junction cancer, hepatocellular carcinoma, malignant pleural mesothelioma, melanoma, non-small cell lung cancer, renal cell carcinoma, squamous cell carcinoma of the head and neck, and urothelial carcinoma.

This document is part of an overall toolkit intended to assist health care providers in optimizing management of patients receiving nivolumab as therapy for their cancer.

DRUG DOSAGE/ADMINISTRATION

- A commonly-prescribed dosage of nivolumab (Opdivo®) is 240 mg administered as an intravenous infusion over 30 minutes every 2 weeks or 480 mg every 4 weeks until disease progression or unacceptable toxicity. **For specifics, the next pages detail dosing in many indications.**
- To illustrate another dosage, adjuvant treatment for patients with melanoma with involvement of lymph nodes (Stage III) or metastatic (Stage IV) disease who have undergone complete resection, the recommended doseage of nivolumab (Opdivo®) is 240 mg administered as an intravenous infusion over 30 minutes every 2 weeks or 480 mg every 4 weeks until disease recurrence or unacceptable toxicity for up to 1 year





- Nivolumab is a clear to slightly opalescent, colorless to pale-yellow solution. Discard the vial if the solution is cloudy, discolored, or contains extraneous particulate matter (other than a few translucent-to-white, proteinaceous particles)
- To prepare the dose, withdraw the required volume of nivolumab and transfer it into an intravenous container. This should be diluted with either 0.9% sodium chloride injection, USP, or 5% dextrose, USP to prepare an infusion with a final concentration ranging from 1 mg/mL to 10 mg/mL
- Mix the diluted solution by gentle inversion. Do not shake
- Do not coadminister nivolumab with other drugs through the same intravenous line
- Nivolumab is classified as an irritant and may be safely administered via a central or peripheral line. It is important to ensure IV access before administration. Nivolumab should be administered through an intravenous line containing a sterile, non-pyrogenic, low-protein-binding in-line or add-on filter (pore size of 0.2-1.2 micrometers)

Dosing & Administration for FDA-approved Indications for Nivolumab

Cancer	Indication	Dosage & Administration
Classical Hodgkin Lymphoma	Adult patients with classical Hodgkin lymphoma that has relapsed or progressed after a autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or 3 or more lines of systemic therapy that includes autologous HSCT	240 mg every 2 weeks or 480 mg every 4 weeks
Colorectal Cancer	Adult and pediatric (12 years and older) patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, as a single agent or in combination with ipilimumab	Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer; adult and pediatric patients weighing 40 kg or greater: 240 mg every 2 weeks or 480 mg every 4 weeks; pediatric patients weighing less than 40 kg: 3 mg/kg every 2 weeks; adult and pediatric patients weighing 40 kg or greater: 3 mg/kg followed by ipilimumab 1 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks
Esophageal Cancer	Adult patients with completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease, who have received neoadjuvant chemoradiotherapy; adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma as first-line treatment in combination with fluoropyrimidine- and platinum-containing chemotherapy; adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma as first-line treatment in combination with ipilimumab; adult patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy	Adjuvant treatment of resected esophageal cancer 240 mg every 2 weeks or 480 mg every 4 weeks for total treatment duration of 1 year; esophageal squamous cell carcinoma 240 mg every 2 weeks or 480 mg every 4 weeks in combination with chemotherapy regimen of fluoropyrimidine- and platinum-containing chemotherapy; 3 mg/kg every 2 weeks or 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks; 240 mg every 2 weeks or 480 mg every 4 weeks
Gastric Cancer, Gastroesophageal Junction Cancer	Adult patients with advanced or metastatic gastric cancer, or gastroesophageal junction cancer in combination with fluoropyrimidine- and platinum-containing chemotherapy	360 mg every 3 weeks with fluoropyrimidine- and platinum-containing chemotherapy every 3 weeks; 240 mg every 2 weeks with fluoropyrimidine- and platinum-containing chemotherapy every 2 weeks
Hepatocellular Carcinoma	Adult patients with hepatocellular carcinoma who have been previously treated with sorafenib in combination with ipilimumab	1 mg/kg followed by ipilimumab 3 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks

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Dosing & Administration for FDA-approved Indications for Nivolumab

Cancer	Indication	Dosage & Administration
Malignant Pleural Mesothelioma	Adult patients with unresectable malignant pleural mesothelioma, as first-line treatment in combination with ipilimumab	360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks
Melanoma	Adult and pediatric (12 years and older) patients with unresectable or metastatic melanoma, as a single agent or in combination with ipilimumab; adjuvant treatment of adult and pediatric patients 12 years and older with completely resected Stage IIB, Stage IIC, Stage III, or Stage IV melanoma	**Adjuvant treatment**: patients weighing 40 kg or greater: 240 mg every 2 weeks or 480 mg every 4 weeks; pediatric patients weighing less than 40 kg: 3 mg/kg every 2 weeks or 6 mg/kg every 4 weeks.
		Unresectable or metastatic melanoma: patients weighing 40 kg or greater: 240 mg every 2 weeks or 480 mg every 4 weeks; pediatric patients weighing less than 40 kg: 3 mg/kg every 2 weeks or 6 mg/kg every 4 weeks; patients weighing 40 kg or greater: 1 mg/kg followed by ipilimumab 3 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks; pediatric patients weighing less than 40 kg: 1 mg/kg followed by ipilimumab 3 mg/kg on the same day every 3 weeks for 4 doses, then 3 mg/kg every 2 weeks or 6 mg/kg every 4 weeks

Dosing & Administration Indications for Nivolumab

Cancer	Indication	Dosage & Administration
Non-small Cell Lung Cancer (NSCLC)	Adult patients with resectable (tumors ≥4 cm or node positive) non-small cell lung cancer (NSCLC) in the neoadjuvant setting, in combination with platinum-doublet chemotherapy; adult patients with resectable (tumors ≥4 cm or node positive) NSCLC and no known EGFR mutations or ALK rearrangements, for neoadjuvant treatment, in combination with platinum-doublet chemotherapy, followed by single-agent nivolumab as adjuvant treatment after surgery; adult patients with metastatic NSCLC expressing PD-L1 (≥1%) with no EGFR or ALK genomic tumor aberrations, as first-line treatment in combination with ipilimumab; adult patients with metastatic or recurrent NSCLC with no EGFR or ALK genomic tumor aberrations as first-line treatment, in combination with ipilimumab and 2 cycles of platinum-doublet chemotherapy; adult patients with metastatic NSCLC and progression on or after platinum-based chemotherapy; patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving nivolumab	**Neoadjuvant treatment of resectable** (tumors ≥4 cm or node positive) NSCLC 360 mg with platinum-doublet chemotherapy on the same day every 3 weeks for 3 cycles; **neoadjuvant and adjuvant treatment of resectable** NSCLC 360 mg with platinum-doublet chemotherapy on the same day every 3 weeks for up to 4 cycles, then continued as single-agent 480 mg every 4 weeks after surgery for up to 13 cycles (~1 year); **metastatic** NSCLC 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks; 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks and 2 cycles of platinum-doublet chemotherapy; 240 mg every 2 weeks or 480 mg every 4 weeks
Renal Cell Carcinoma	Adult patients with intermediate or poor risk advanced renal cell carcinoma, as a first-line treatment in combination with ipilimumab; adult patients with advanced renal cell carcinoma, as a first-line treatment in combination with cabozantinib; adult patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy	3 mg/kg followed by ipilimumab 1 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks; 240 mg every 2 weeks or 480 mg every 4 weeks administered in combination with cabozantinib 40 mg once daily without food; 240 mg every 2 weeks or 480 mg every 4 weeks
Squamous cell carcinoma of the head and neck	Adult patients with recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy	240 mg every 2 weeks or 480 mg every 4 weeks
Urothelial Cancer	Adjuvant treatment of adult patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection of UC; adult patients with unresectable or metastatic urothelial carcinoma, as first-line treatment in combination with cisplatin and gemcitabine; adult patients with locally advanced or metastatic urothelial carcinoma who: have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy	**Adjuvant treatment** of urothelial carcinoma 240 mg every 2 weeks or 480 mg every 4 weeks; first-line **unresectable or metastatic** urothelial carcinoma 360 mg every 3 weeks with cisplatin and gemcitabine on the same day for up to 6 cycles, then 240 mg every 2 weeks or 480 mg every 4 weeks; **previously treated locally advanced or metastatic** urothelial carcinoma 240 mg every 2 weeks or 480 mg every 4 weeks

SIDE EFFECTS AND THEIR MANAGEMENT

Because nivolumab is an immunotherapy that works by enhancing the patient's immune system, most adverse reactions associated with nivolumab are related to overactivity of the patient's immune system (ie, immune-related adverse events [irAEs]). Various organ systems (often more than one) or tissues may be affected.

- Keys to toxicity management:
  - » Proactive assessment for early signs/symptoms of irAEs
  - » Prompt intervention
  - » irAEs are typically managed with dose interruption and selective use of corticosteroids
  - » In rare instances, toxicity may be steroid refractory, and additional immunosuppressive agents (infliximab, mycophenolate mofetil, cyclophosphamide, etc) may be necessary
  - » Nivolumab will likely be held or discontinued depending on the severity and/or persistence of the irAE
  - » Referral to organ specialist should be considered, given that unique testing and management strategies may be required
- irAEs associated with nivolumab treatment can be categorized as those that are most common, less common but serious, and others that are easily overlooked
- Table 1 lists these irAEs and the corresponding Care Step Pathways in Appendix 1. Other adverse events associated with nivolumab are shown in Appendix 2

Table 1. Care Step Pathways for the management of immune-related AEs associated with nivolumab monotherapy.

irAE category	Examples
Most common	Skin toxicities (pruritus, rash, etc) Gastrointestinal toxicity: Diarrhea/colitis Thyroiditis Hepatic toxicities
Less common but serious	Additional endocrinopathies Hypophysitis (pituitary) Adrenal insufficiency Diabetes Pneumonitis
Easily overlooked	Arthralgia/arthritis Mucositis/xerostomia Nephritis

Management of other AEs associated with nivolumab monotherapy

Adverse event	Common symptoms	Common management/anticipatory guidance
Anorexia	Decreased appetite	• Monitor weight; query patient about appetite/eating habits; advise dietary modification if necessary (should improve with time) • Anticipate standard dose holds/discontinuations* • Consider referral to nutrition services for counseling on best food choices to avoid excessive weight loss
Constipation/ abdominal pain	Infrequent stools/ difficulty stooling, abdominal pain	• Consider other causes, such as opioid-induced constipation • Increase fluid, fiber; use laxatives with caution; suggest stool softeners and increased physical activity • Consider appropriate testing to evaluate bowel obstruction • Anticipate standard dose holds/discontinuations* for Grade 3 and Grade 4 (constipation with manual evacuation indicated, severe abdominal pain, or life-threatening consequences)
Embryo-fetal toxicity	—	• Advise patients to tell their HCPs immediately if they or their partners suspect they are pregnant while taking therapy • Advise patient to tell HCP immediately if they or their partner suspect they are pregnant while taking therapy
Encephalitis	Headache, fever, tiredness, confusion, memory problems, sleepiness, hallucinations, seizures, stiff neck	• New-onset, moderate-to-severe symptoms: rule out infectious or other causes • Counsel neurologist, obtain brain MRI, and lumbar puncture • Anticipate standard dose-holds and discontinuations*
Fatigue	Feeling tired; lack of energy	• Query patients regarding energy level; evaluate possible contributory factors, including infection, disease progression, and hematological and metabolic abnormalities; standard supportive care • Anticipate standard dose holds/discontinuations* • Fatigue that interferes with ADLs is concerning and should be evaluated for underlying causes, such as possible endocrinopathy
Headache	Head pain	• Need to rule out brain metastases, encephalitis, or hypophysitis; otherwise, standard supportive care (should improve with time) • Headache occurring in conjunction with fatigue could be indicative of hypophysitis; obtain MRI of brain with pituitary slices/pituitary protocol to confirm/rule out. • Anticipate standard dose holds/discontinuations*

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Management of other AEs associated with nivolumab monotherapy

Adverse event	Common symptoms	Common management/anticipatory guidance
Infusion reaction	Chills/shaking, back pain, itching, flushing, difficulty breathing, hypotension, fever	• For mild/moderate (Grade 1-2) reactions: interrupt or slow rate of infusion; monitor to recovery • For severe/life-threatening (Grade 3-4) reactions: discontinue nivolumab; manage anaphylaxis via institutional protocol; monitor. Premedication with an antipyretic and antihistamine may be considered for future doses
Insomnia	Difficulty falling or staying asleep	• Counsel patients on good sleep habits; prescription medications can be used if needed (should improve over time) • Anticipate standard dose holds/discontinuations*
Myocarditis	Shortness of breath; arrhythmia; light-headedness; chest pain; fatigue; nausea; edema	• Obtain baseline ECG • Assess cardiac biomarkers (BNP; troponin) • Control cardiac diseases (and risk factors) optimally • Consult cardiologists and consider corticosteroids if myocarditis is suspected • Add additional immunosuppressive agents in severe, refractory cases • Institute standard dose holds/discontinuations (in consultation with cardiologist)
Nausea/vomiting	Vomiting, queasiness, RUQ or LUQ pain	• Rule out brain metastases and gastroenteritis • Provide standard supportive care, since it is adequate in most cases • Check LFTs/lipase/amylase if hepatotoxicity or pancreatitis is suspected • Anticipate standard dose holds/discontinuations*
Upper respiratory tract infection	Cough, runny nose, sore throat, nasal congestion	• Evaluate potential causes—a dry cough and shortness of breath would increase concern for pneumonitis • Standard supportive care • Anticipate standard treatment holds*
Vision changes	Eye redness, pain, blurred vision, photophobia	• Test and evaluate for uveitis and episcleritis (by ophthalmologist, preferably) • Urgency of ophthalmology referral increases with grade • G1: continue immunotherapy, use artificial tears • G2: hold immunotherapy; ophthalmic and systemic corticosteroids (under ophthalmologist guidance) • G3 or G4: permanently discontinue immunotherapy; treatment by ophthalmologist to include ophthalmic and systemic corticosteroids

*Withhold nivolumab for any Grade 3 (severe) AE. Permanently discontinue for any Grade 4 (life-threatening) AE, persistent Grade 2-3 AE, any severe (Grade 3) AE that recurs, or when ≥10 mg/d prednisone or equivalent is required for 12 weeks. Resume treatment when AE returns to Grade 0 or 1.

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CLINICAL PEARLS

- It is important to monitor laboratory values at the start of treatment, periodically during treatment, and as indicated clinically. Laboratory values commonly monitored include: CBC w/ differential, creatinine, alkaline phosphatase, AST/ALT, bilirubin (direct/total), sodium, potassium, calcium, magnesium, thyroid function, and glucose. Please see the individual irAE CSPs for more detail about specific laboratory monitoring
- Nivolumab-related irAEs may occur at any time, including after treatment completion or discontinuation
- Patients sometimes experience signs/symptoms that they think are due to “flu” or a cold, but that actually represent an irAE or an infusion reaction
- Endocrinopathies often present with vague symptoms (fatigue, headache, and/or depression) that can easily be overlooked or initially misdiagnosed. Hypervigilance and follow-up is important on the part of both HCPs and patients
- Endocrinopathies tend to occur somewhat more commonly with nivolumab or other PD-1 inhibitor therapies than with ipilimumab monotherapy
- Unlike other irAEs, endocrinopathies usually do not resolve and may require lifelong hormone replacement therapy
- IrAEs have different time courses. New irAEs may become apparent upon tapering of corticosteroids used to treat an earlier onset irAE, since the new irAE can be suppressed or masked by immunosuppressive therapy. Therefore, during the taper period, patients should be advised to be on the lookout for early signs of new irAEs as well as recurrence of the original irAE that was being treated
- HCPs should encourage patients to carry information about their nivolumab regimen with them at all times. This might be the nivolumab-specific wallet card, or at least emergency phone numbers and a list of side effects associated with the regimen. You may suggest that they paperclip the wallet and insurance cards together so information about their regimen will be shared whenever they show the insurance card
- Advise patients to take pictures of any skin changes for documentation

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QUESTIONS & ANSWERS

Q. How long will patients stay on nivolumab?

A. The prescribing information indicates until disease progression or unacceptable toxicity. The interpretation of these criteria varies from institution to institution and from provider to provider.

Q. Are there standard dosage reductions for irAEs associated with nivolumab?

A. There are no dosage reductions for irAEs associated with nivolumab. The dose is either held until the irAE resolves sufficiently (typically to Grade 0 or Grade 1) or, if the irAE is severe enough, nivolumab is discontinued permanently.

Q. Does the safety profile of nivolumab vary when used in different tumor types?

A. Generally, the safety profile of nivolumab is similar across tumor types. However, the context may be different—patients with other tumor types may have differing comorbidities or underlying organ dysfunction. For example, lung cancer patients may have underlying lung disease that will exacerbate shortness of breath associated with pneumonitis. In addition, patients with melanoma may have a higher incidence of vitiligo development.

Q. How do I counsel my patients about immunizations?

A. That's a logical question, given that the checkpoint inhibitors alter the immune response. Advise your patients not to receive live vaccines (eg, measles, mumps, and rubella and the varicella vaccine) because they have not been evaluated in this setting. The use of attenuated vaccines has been and continues to be evaluated. Counsel patients to discuss all immunizations with the oncology team prior to administration so the benefits and risks can be weighed on an individual basis. For example, SHINGRIX®, approved in 2017, is an attenuated (non-live) varicella vaccine; its use can be discussed with the oncology team if a recommendation is being made for the patient to receive the injection series. Annual influenza vaccination with the inactivated influenza vaccine is recommended. The nasal spray flu vaccine is a live attenuated influenza vaccine and should not be administered to patients treated with immune checkpoint inhibitors.

Q. What are the differences between oxaliplatin-induced peripheral neuropathy (PN) and nerve problems see with nivolumab?

A. Oxaliplatin PN tends to happen on the hands and feet with tingling and numbness. Nivolumab-induced nerve problems manifest as weakness and difficulty walking, but can also manifest with worsening numbness/tingling/functional impairment. It is imperative to ascertain baseline neurological deficits prior to initiating nivolumab for appropriate evaluation of worsening symptoms. For careful evaluation of worsening symptoms during therapy or after discontinuation accurate assessment of neuropathy may require patient demonstration (buttoning shirt, walking, testing grip).

Q. How do we test for MSI and MMR?

A. PCR for MSI and IHC for MMR can be requested to identify patients appropriate for treatment with nivolumab. Your pathologist may be able to perform the testing in your hospital/laboratory or may need to request testing from a reference lab.

Q. How is a nivolumab-induced rash different from an EGFR-induced rash seen with cetuximab or panitumumab?

A. Generally, an EGFR-induced rash manifests earlier, is more macular-papular, and less puritic, and responsive to the STEPP skin protocol. A rash induced by nivolumab tends to be more pruritic, accompanied by a tightness/burning sensation, not acne-like, and generally responsive to oral corticosteroids.

Q. I have experience using nivolumab for lung cancer. Is the safety profile different in those patients' vs HNSCC patients?

A. Generally, the safety profile of nivolumab is similar across tumor types. However, the context may be different—patients with other tumor types may have differing comorbidities or underlying organ dysfunction. For example, lung cancer patients may have underlying lung disease that will exacerbate shortness of breath associated with pneumonitis.

Q. Can nivolumab be administered safely in patients with HCC who are hepatitis B or hepatitis C positive?

A. As is the case with sorafenib, nivolumab can be safely administered in patients who are hepatitis B or hepatitis C positive without any dose reductions as long as the synthetic function of the liver is acceptable.

Q. Can nivolumab be given safely to patients with liver impairment?

A. As with sorafenib, nivolumab can be given to patients whose Child-Pugh score is A or B (used to evaluate chronic liver disease and cirrhosis). However, careful monitoring of liver function is critical.

ADDITIONAL RESOURCES

- Boutros C, Tarhini A, Routier E, et al. Safety profiles of anti-CTLA-4 and anti-PD-1 antibodies alone and in combination. *Nat Rev Clin Oncol*. 2016;13:473-486.
- Brahmer JR, Lacchetti C, Schneider BJ, et al. Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol.* 2018;36:1-60.
- Dadu R, Zobniw C, Diab A. Managing adverse events with immune checkpoint agents. *Cancer J*. 2016;22:121-129.
- Friedman CF, Proverbs-Singh TA, Postow MA. Treatment of the immune-related adverse effects of immune checkpoint inhibitors: a review. *JAMA Oncol*. 2016;2:1346-1353.
- Kumar V, Chaudhary N, Garg M, Floudas CS, Soni P, Chandra AB. Current diagnosis and management of immune related adverse events (irAEs) induced by immune checkpoint inhibitor therapy. *Front Pharmacol*. 2017;8:49. doi: 10.3389/fphar.2017.00049
- McGettigan S, Rubin KM. Managing adverse events with PD-1 inhibitor therapy of advanced melanoma: consensus statements from the faculty of the Melanoma Nursing Initiative. *Clin J Oncol Nurs.* 2017;21(Suppl):42-51.
- Naidoo J, Page DB, Li BT, et al. Toxicities of the anti-PD-1 and anti-PD-L1 immune checkpoint inhibitor antibodies. *Ann Oncol*. 2015;26:2375-2391.
- National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Management of Immunotherapy-Related Toxicities. Version 1.2018. Fort Washington, PA: National Comprehensive Cancer Network; 2018.
- Nishijima TF, Shachar SS, Nyrop KA, Muss HB. Safety and tolerability of PD-1/PD-L1 inhibitors compared with chemotherapy in patients with advanced cancer: a meta-analysis. *Oncologist*. 2017;22:470-479.
- Opdivo® [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2017. Available at: http://packageinserts.bms.com/pi/pi_opdivo.pdf

ADDITIONAL RESOURCES

- Opdivo patient alert card (wallet card) and other resources. http://www.opdivo.com/servlet/ servlet.FileDownload?file=00P1Y00000v60IZUAY
- Puzanov I, Diab A, Abdallah K, et al. Managing toxicities associated with immune checkpoint inhibitors: consensus recommendations from the Society for Immunotherapy of Cancer (SITC) Toxicity Management Working Group. *J Immunother Cancer*. 2017;5:95. doi: 10.1186/s40425-017-0300-z
- Spain L, Diem S, Larkin J. Management of toxicities of immune checkpoint inhibitors. *Cancer Treat Rev*. 2016;44:51-60.
- Villadolid J, Amin A. Immune checkpoint inhibitors in clinical practice: update on management of immune-related toxicities. *Transl Lung Cancer Res*. 2015;4:560-577.
- Weber JS, Postow M, Lao CD, Schadendorf D. Management of adverse events following treatment with anti-programmed death-1 agents. *Oncologist*. 2016;21:1230-1240.

PATIENT RESOURCES

ADDITIONAL INFORMATION RESOURCES

AIM at Melanoma Foundation (Ask an Expert program, patient symposia, drug resources, etc)
https://www.aimatmelanoma.org/

American Cancer Society
https://www.cancer.org/

FINANCIAL ASSISTANCE

BMS Access Support
1 (800) 861-0048
http://www.bmsaccesssupport.bmscustomerconnect.com/patient

Cancer Financial Aid Coalition
Facilitates communication, educates and advocates for patients.
www.cancerfac.org

Centers for Medicare and Medicaid Services (CMS)
Apply to determine if you are eligible for government assistance. www.cms.gov or www.medicare.gov
800-633-4227

Lazarex Foundation
Provides assistance with travel costs for clinical trial participation. Ask your social work counselor for a referral if you have been consented to a clinical trial for melanoma.
www.lazarex.org

Needymeds
Database to search for free or low-cost medications, help with medical transportation and other resources.
www.needymeds.org

Patient Advocate Foundation
Provides assistance with mediation, financial stability, and other assistance. Funds subject to availability. Patient must meet their eligibility for financial assistance.
www.patientadvocate.org
800-532-5274

The Sam Fund for Young Adult Survivors of Cancer
Assists cancer survivors ages 21-39 with their transition into post-treatment life. This program distributes grants and scholarships in an effort to enable survivors to pursue goals.
www.thesamfund.org
info@thesamfund.org

PRESCRIPTION ASSISTANCE

CancerCare Co-Payment Assistance Foundation
Helps with the cost of medication. Availability of funds for patients subject to availability.
www.cancercarecopay.org
1-866-552-6729

Medicine Assistance Tool
Database to search for patient assistance resources offered by pharmaceutical companies.
www.medicineassistancetool.org/

Patient Advocate Foundation Co-Pay Relief
Provides direct financial support to patients who medically qualify. Availability of funds for patients subject to availability.
www.copays.org
1-866-512-3861

Good Days
Formerly known as the Chronic Disease Fund. Provides assistance with insurance co-pays, and prescription medications. Availability of funds for patients subject to availability.
www.mygooddays.org

HealthWell Foundation
For patients who cannot afford insurance premiums, co-payments, co-insurance, or other out-of-pocket health care costs. Availability of funds for patients subject to availability. Patient must also meet eligibility for financial assistance.
www.healthwellfoundation.org or
grants@healthwellfoundation.org
1-800-675-8416

The Assistance Fund, Inc
Provides prescription copay and financial assistance, including health insurance premiums. Availability of funds for patients subject to availability.
www.theassistancefund.org
1-855-845-3663

PAN Foundation
Provides financial assistance to cover out-of-pocket treatment costs. Availability of funds for patients subject to availability.
www.panfoundation.org
1-866-316-PANF (7263)

Patient Assistance Program
Comprehensive database of patient assistance programs offering free medications.
www.rxassist.org
info@rxassist.org

HOUSING

American Cancer Society – Hope Lodge
Provides free housing during treatment appointments. Requires a referral from your social worker.
www.cancer.org/
1-800-227-6333

TRANSPORTATION (AIR AND GROUND)

Medicaid
Ground transportation only. Sets up rides and provides mileage reimbursement for Medicaid patients only.
1-877-633-8747

Mercy Medical Angels
Provides free medical transportation (flights, gas cards, bus and train tickets) for patients with financial needs who need to travel more than 50 miles. Patients must meet their eligibility for financial assistance.
www.mercymedical.org/

Pilots for Patients
Provides free flights to people in need of medical treatment. Patient must be medically stable to fly and be ambulatory. Ask your social worker about a referral.
www.pilotsforpatients.org
318-322-5112