ABSTRACT

Immune checkpoint inhibitors have revolutionized the treatment of cancer and are now omnipresent. However, immune-related adverse events can present with varying phenotypes and timing, which can pose diagnostic and therapeutic challenges for the treating oncologist as well as subspecialty consultants. Biopsies of affected organs may provide insight into biologic mechanisms as well as potentially guide management in certain circumstances.

Treatment with immune checkpoint inhibitors (ICIs) continues to transform oncology and includes antibodies against CTLA-4, PD-1, and PD-L1. Anticancer benefit has been shown across multiple solid tumor malignancies as well as in some hematologic malignancies. Furthermore, these agents are being combined with other anticancer agents, including cytotoxic chemotherapies, molecularly targeted therapies, and radiation. The adverse effects of ICIs are distinct from other cancer treatments and management continues to evolve. The toxicities are related to immune stimulation and/or attack on various organs and systems and are termed immune-related adverse events (irAEs). IrAEs are often unpredictable and can range from asymptomatic laboratory abnormalities to life-threatening diagnoses requiring hospitalization and specialized treatments. Although these appear to resemble autoimmune conditions, irAEs are distinct and more expansive. They can impact one or several organs, with the ICI agent and its dosing and combination with other agents impacting the rate and severity of irAEs. The mainstay of management is an oral or intravenous glucocorticoid with a slow taper, typically over no less than 4 weeks, and in most cases this will lead to complete resolution of the toxicity.

However, irAEs may resemble other serious issues, such as infections, cancer progression, or other inflammatory processes, for which bloodwork and radiologic imaging may not secure the diagnosis. Challenges to studying irAEs include the varied timing and severity of presentations, treatment regimens, and oncologic diagnoses; the distinct organs impacted; and variable management strategies. Thus, much has been learned from irAE case reports and retrospective case series including pathologic specimens, such as biopsies obtained during clinical care and autopsies. Biopsies may serve to guide important aspects of care, such as supporting or rejecting an immune-mediated process as the cause of the sign/symptom, providing information regarding another or additional cause of the sign/symptom, and providing information regarding irAE severity, duration (acute vs chronic), or resolution. This information may assist in
toxicity management, such as the dosing/tapering of steroids, the addition of other immune-suppressing agents, and whether to rechallenge with ICIs. Although very few laboratory or pathologic findings definitively rule in or out many of these irAEs, pathologic studies advance our understanding of these toxicities and evolve their management. This review discusses the role of tissue biopsies in the management of suspected irAEs in conjunction with subspecialty consultants. Organs reviewed include colon, liver, lung, heart, and kidney. Skin irAEs and skin biopsy are excluded, because skin biopsies are often easier to facilitate by the practicing oncologist and have varied and complex pathologic findings that are beyond the scope of this article.

Colon
Diarrhea is common, and estimated to occur in 5% to 20% of patients receiving PD-1/PD-L1 antagonists, and 20% to 45% of those receiving CTLA-4 antagonists alone or in combination with PD-1 agents.\(^2\)–\(^3\) Diarrhea often presents 1 to 2 months after CTLA-4 inhibitor initiation and 2 to 3 months after PD-1/PD-L1 inhibitor initiation. Biopsy-proven colitis is rarer, occurring in 3% to 16% of patients treated with CTLA-4 antagonists alone or in combination with PD-1 antagonists, and 1% to 4% of patients receiving PD-1/PD-L1 antagonist monotherapy. The mechanisms underlying colitis are unclear but may involve interferon-γ-producing CD8\(^+\) T cells.\(^4\)–\(^5\)

Evaluation is predicated on clinical history and laboratories, often with confirmation by endoscopically obtained biopsies\(^6\) (Figures 1 and 2). Stool studies can distinguish infection from ICI-induced colitis, given that both can present with a similar clinical picture. Infection can be assessed by gastrointestinal (GI) PCR or stool culture and ova and parasite studies. Inflammation can be assessed by fecal calprotectin (FCP) or lactoferrin assays. FCP and lactoferrin are antimicrobial peptides released by activated neutrophils. Because neutrophils are a defining feature of acute inflammation, elevated FCP and lactoferrin levels have high sensitivity and specificity for intestinal inflammation from any cause. FCP offers approximately 90% sensitivity and specificity for active colitis in inflammatory bowel disease (IBD). Even though the underlying pathogenesis of ICI-induced colitis and IBD may be different, neutrophils are a feature of both, suggesting that FCP will also have high sensitivity and specificity in ICI-induced colitis.

Endoscopy with biopsy should be considered for any suspicion of ICI-induced colitis, and especially for grade \(\geq 2\)\(^6\)–\(^9\) (Table 1). Histologic findings compatible with ICI-induced colitis include acute inflammation with lymphocytosis, neutrophil infiltrates, crypt abscesses, and epithelial cellular apoptosis. The inflammatory infiltrates often encompass multiple cell types, including T lymphocytes, eosinophils, and plasma cells, and a subset may have features of lymphocytic colitis or manifest with chronic changes, including distortion of the crypt architecture, granulomas, and Paneth cell metaplasia. The left colon is typically affected, with isolated right colonic involvement seen in a minority of patients.\(^6\) Thus, flexible sigmoidoscopy with or without conscious sedation is sufficient in most cases. Sigmoidoscopy spares the patient a bowel preparation, confers a lower risk of perforation, and typically can be performed with lower levels of sedation, therefore offering significant advantages over colonoscopy with little loss of diagnostic yield. Importantly, the endoscopic appearance is highly variable and can be grossly normal, and may not correspond with clinical severity. Therefore, mucosal biopsies are recommended even if the colon appears normal on visual inspection. Biopsies, particularly performed in the rectum and sigmoid, are associated with a negligible risk of bleeding or perforation.

GI PCR and FCP (or alternatively stool culture, ova and parasite assay, plus lactoferrin) should be considered in all patients who initially present with diarrhea, and flexible sigmoidoscopy should be performed in those strongly suspected of having ICI-induced colitis. In practice, there are often delays in scheduling endoscopy. Thus, an elevated FCP level with a negative GI PCR result is highly suggestive of ICI-induced colitis, and initiation of steroid therapy may be warranted in these patients. Biopsy confirmation of colitis can be useful if inadequate response to steroid therapy warrants additional investigation or use of additional agents, such as infliximab or vedolizumab, to control GI irAEs. Consultation with a gastroenterologist is always preferred to help ensure alternative etiologies are considered and excluded.

Liver
The incidence of ICI liver injury varies widely (<1%–15%), depending on the use of a CTLA-4 antagonist or PD-1/PD-L1 antagonist alone or in combination.\(^10\) ICI-induced hepatitis is usually asymptomatic and detected within the first 4 to 16 weeks of treatment via preinfusion laboratory monitoring. To establish a clinical diagnosis, competing causes of liver injury should be excluded through medical history (eg, use of alcohol, acetaminophen, nutritional supplements, or other potential hepatotoxins); serologic testing for viral hepatitis, muscle injury, or alcohol; and contrast-enhanced CT or MRI imaging of the liver in select patients (Figure 3). Grade 3/4 liver injury occurs in 1% to 3% of treated patients, but jaundice and liver failure are exceedingly uncommon.\(^7\) In clinical trials, most ICI-induced hepatitis demonstrated an acute hepatocellular injury pattern with a predominance of aspartate transaminase and alanine transaminase elevation; however, in clinical practice, most patients (70%) have a mixed or cholestatic injury pattern, and most liver injury cases are attributable to tumor progression and/or hepatic metastases.\(^11\)–\(^12\)
There are no histopathologic features pathognomonic for ICI-induced hepatitis. Furthermore, the timing of a liver biopsy in relationship to ICI cessation and initiation of steroids in published reports is heterogeneous, making clinical interpretation difficult. Adequate tissue for diagnostic evaluation can be safely obtained in most patients via percutaneous biopsy with a 1% risk of bleeding, whereas transjugular biopsies are generally reserved for patients with underlying coagulopathy or ascites (Table 1). In one study of 16 patients with ICI-induced hepatitis, liver biopsy demonstrated granulomatous hepatitis with fibrin deposits in 5 patients who had received CTLA-4 antagonists.13 Other studies have demonstrated microgranulomas, lobular hepatitis, and periportal inflammation with varying degrees of necrosis.13–15 One study demonstrated that 95 of the 107 (89%) patients with grade 3 hepatitis (based on laboratory assessment) who underwent a liver biopsy had findings compatible with ICI-induced hepatitis, but 5.3% had no hepatic inflammation.16 Prior to the biopsy, 59% of patients had received steroids, whereas after the biopsy 92% received steroids. The biopsies were obtained at a median of 5 days after grade 3 ICI-induced hepatitis onset, and 2 patients had major complications from the biopsy procedure. Among the 12 patients without ICI-induced hepatitis, 4 had malignant biliary obstruction, 4 had drug-induced liver injury from another drug, and 2 had unsuspected malignant infiltration of the liver. The patients with non–ICI-induced hepatitis were more likely to be jaundiced and to have failed to respond to prior steroid treatment. Interestingly, the histology of ICI-induced hepatitis is distinct from that of autoimmune hepatitis, wherein plasmacytosis and a predominance of CD20+ and CD4+ lymphocytes is seen.10 In addition, patients with ICI-induced hepatitis are not predominantly female, <50% have detectable serum autoantibodies, and few have elevated immunoglobulin levels.

Figure 1. Recommended evaluation of patients with grade 1/2 diarrhea receiving immunotherapy.

Abbreviations: EGD, esophagogastroduodenoscopy; FCP, fecal calprotectin; GI, gastrointestinal; IBS, irritable bowel syndrome.
All patients with grade ≥2 liver injury should undergo a contrast-enhanced CT or MRI of the liver to exclude liver metastases and/or pancreaticobiliary disease. If the imaging is negative or demonstrates stable disease, hepatology referral is recommended for further medical evaluation and consideration of liver biopsy concomitant with or prior to initiation of high-dose corticosteroids and prior to antimetabolite therapy. A liver biopsy in nonresolving suspected ICI-induced hepatitis may provide prognostic information as well as avoid excessive immunosuppression in those patients with an alternative cause of liver injury.

**Lung**

ICI-induced pneumonitis (ICIP) occurs in approximately 5% to 19% of patients receiving ICI therapy. The incidence is higher with dual immune checkpoint inhibition in patients with interstitial lung disease and with advanced non–small cell lung cancer. The biologic mechanisms for development of ICIP are poorly understood, but may involve increased inflammatory cytokines/complement-mediated inflammation and increased T-cell activity against autoantigens.

The diagnosis of ICIP is one of exclusion and is typically made based on symptoms, signs, and clinical imaging. Patients often present with a progressive dry cough and shortness of breath, and may be hypoxic. Although chest CT imaging is critical for diagnosis, there is no pattern of parenchymal infiltrates that is pathognomonic for ICIP. Often lung opacities are characterized as cryptogenic organizing pneumonia pattern, interlobular septal thickening, ground glass opacities, hypersensitivity pattern, and not

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**Figure 2.** Recommended evaluation of patients with grade 3/4 diarrhea receiving immunotherapy. Abbreviations: EGD, esophagogastroduodenoscopy; FCP, fecal calprotectin; GI, gastrointestinal.
Biopsy for Immune Checkpoint Toxicity

Table 1. Summary Table

<table>
<thead>
<tr>
<th>Target Organ</th>
<th>Colon</th>
<th>Liver</th>
<th>Lung</th>
<th>Heart</th>
<th>Kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical symptoms</td>
<td>Diarrhea, cramping, nausea, and/or vomiting</td>
<td>Asymptomatic, jaundice, fatigue</td>
<td>Shortness of breath, cough, fever</td>
<td>Asymptomatic, chest pain, shortness of breath, palpitations, fatigue</td>
<td>Asymptomatic leg edema if nephrotic, fever</td>
</tr>
<tr>
<td>Median time to onset</td>
<td>6 wk$^{50}$</td>
<td>6–12 wk$^{51}$</td>
<td>34 wk$^{19,52}$</td>
<td>6 wk$^{52}$</td>
<td>14 wk$^{52}$</td>
</tr>
<tr>
<td>Medical evaluation</td>
<td>Fecal calprotectin, GI PCR</td>
<td>Diagnostic serologies, contrast-enhanced CT</td>
<td>Sputum studies, chest CT</td>
<td>Troponin, CK, BNP, EKG, echocardiogram, cardiac MRI</td>
<td>Urinalysis</td>
</tr>
<tr>
<td>Tissue biopsy technique</td>
<td>Flexible sigmoidoscopy ± EGD with biopsy</td>
<td>Percutaneous liver biopsy$^a$</td>
<td>Bronchoscopy with TBBx and BAL</td>
<td>Endomyocardial biopsy</td>
<td>Percutaneous renal biopsy</td>
</tr>
<tr>
<td>Risks</td>
<td>&lt;1% risk of bleeding$^{19}$</td>
<td>0.5% bleeding$^{54}$</td>
<td>2.8% bleeding, hypoxia, pneumothorax$^{27}$</td>
<td>&lt;1% myocardial perforation, tamponade, arrhythmias$^{55}$</td>
<td>1.2% bleeding$^{16}$</td>
</tr>
</tbody>
</table>

Abbreviations: BAL, bronchoalveolar lavage; BNP, B-type natriuretic peptide; CK, creatine kinase; EGD, esophagogastroduodenoscopy; EKG, electrocardiogram; GI, gastrointestinal; TBBx, transbronchial lung biopsy. $^a$Transjugular reserved for those with INR >1.5 and platelets <$60 \times 10^3/\mu L$ or ascites.

otherwise specified.$^{19}$ The differential diagnosis is broad and may include infectious etiologies (tuberculosis, aspergillosis, cytomegalovirus pneumonia, *Pneumocystis jirovecii* pneumonia), nonmalignant cardiopulmonary disease, lymphangitic carcinomatosis, and tumor pseudo-progression. One case series identified concomitant pneumonia, volume overload, other drug or radiation pneumonitis, alveolar hemorrhage, and pulmonary embolus.$^{21}$

Transbronchial lung biopsy may assist in ruling out confounding conditions such as infection, granulomatous disease, and lymphangitic tumor progression (Table 1). Biopsies may also confirm the presence of fungal organisms, including *Aspergillus*, *Blastomyces*, *Histoplasma*, or *Candida*, and fungal infections such as mucormycosis. Histopathologic characteristics of ICIP have been incompletely described; however, sarcoid-like granulomatous lung reaction, interstitial fibrosis/pneumonitis, diffuse alveolar hemorrhage, and organizing pneumonia have been reported.$^{19,22}$ A case series of 6 patients who underwent transbronchial lung biopsies found inflammatory and lymphocytic infiltration.$^{23}$ A recent report of 7 patients with ICIP identified organizing pneumonia, foamy macrophages, and pneumocyte vacuolization in all histopathologic reviews, with a few demonstrating non-necrotizing airspace granulomas.$^{24}$ Two fatal cases of ICIP noted acute fibrinous pneumonitis and diffuse alveolar damage on pathologic review. Finally, a review of 20 patients with ICIP who had transbronchial lung biopsies revealed lymphocytic infiltrates (mostly T cells, with a predominance of CD8$^+$ cells) and granulomas.$^{25}$ These results are intriguing and worthy of further study, but are unfortunately not readily translatable to clinical practice.

Bronchoalveolar lavage (BAL) fluid is presently of limited value in confirming ICIP. Small studies have suggested that lymphocytosis, an increase in central memory T cells, and possibly an elevated CD4$^+$/CD8$^+$ ratio are associated with pneumonitis.$^{26}$ Another case series noted T-lymphocytic alveolitis in 24 of 35 patients who underwent BAL. Two studies noted a mean BAL lymphocyte count of 14% to 34%.$^{18,23}$ However, there are no cytopathologic features that will confirm ICIP, and this procedure is mainly used to rule out infections.

The roles of transbronchial lung biopsy and BAL have not been established to confirm ICIP and are not routinely recommended. However, they remain important diagnostic modalities when there is clinical suspicion for infection or progressive malignancy, with or without ICIP, that would significantly change the management. The risks of BAL and transbronchial lung biopsy are generally low and include significant bleeding in 1% to 2.8% of cases, pneumothorax in 4%, and hypoxia/bronchospasm in 9%.$^{27}$ Shared decision-making with patients is essential to review the risks/benefits value of this procedure for pulmonary infiltrate evaluation.

**Heart**

Myocarditis is an infrequent yet potentially life-threatening irAE. ICI myocarditis (ICIM) is estimated to occur in 0.5% to 1.5% of patients, with most events occurring in the first 30 days after initiation of ICI therapy.$^{28,29}$ Mortality of patients hospitalized for ICIM is high, ranging from 25% to 46%. The clinical presentation of ICIM is highly variable and encompasses a wide range of symptoms, laboratory markers, imaging, and electrocardiographic abnormalities. This makes diagnosis of ICIM challenging.$^{30,31}$ Patients may exhibit different combinations of electrocardiographic changes, arrhythmias, decreased left ventricular ejection fraction, or delayed
gadolinium enhancement on cardiac MRI. However, the most consistent feature of ICIM is the evidence of myocardial injury, noted as a persistent elevation in cardiac troponins.

Endomyocardial biopsy (EMB) may help in the diagnosis of unexplained cardiomyopathies, including myocarditis, and is used to monitor cardiac transplant rejection (Table 1). EMB is typically performed via internal jugular or femoral vein access in conjunction with fluoroscopic and echocardiographic guidance to sample tissue from the right ventricular septum, where the risk of cardiac perforation and stroke is minimized. Technical advances and more widespread expertise have made EMB a relatively safe procedure at higher volume centers, with a <1% risk of major complications. Unfortunately, the diagnostic yield, sensitivity, and specificity

Figure 3. Recommended evaluation of patients with grade 3/4 hepatotoxicity receiving immunotherapy. Immunotherapy should be held in all patients with ALT/AST >5x ULN or baseline (ie, grade 3). A methylprednisolone dose of 1 to 1.5 mg/kg/d is recommended in patients who do not respond, as well as hepatology consultation for consideration of liver biopsy. Patients with grade 4 liver injury should be hospitalized to facilitate evaluation and treatment, as well as any patient with a total bilirubin >2.5 mg/dL.

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HV, hepatic vein; INR, international normalized ratio; PV, portal vein; TBIL, total bilirubin; ULN, upper limit of normal.
of EMB are highly variable and depend on the type of biopsy (right ventricular, left ventricular, or biventricular), the sampling rate, and the extent of underlying myocardial disease (patchy vs extensive). The major limitation of EMB is sampling error, notably for diseases with patchy involvement of the myocardium, such as myocarditis. Among 1,230 patients presenting with unexplained cardiomyopathy, EMB yielded a diagnosis in only 15% of patients, albeit no immunohistochemical or molecular techniques for viral genome analyses were used. In a more recent study that included patients with suspected myocarditis, the sensitivity of EMB was higher, with 43.6% of patients having histologic findings of myocarditis.

The role of EMB in ICIM is still being defined. Histologic staging of non-ICIM severity according to the Dallas criteria relies on the extent of inflammatory cell infiltrate and myocyte loss. Whether the Dallas criteria can be applied to ICIM is unclear. Histopathologic findings described in ICIM consist of infiltrating CD4+ and CD8+ T cells and CD68+ macrophages along with intense PD-L1 staining, but relatively less myocyte loss than expected in non-ICIM. One case series suggested that patients with suspected ICIM and high-grade features on histology had poor outcomes. In a more recent study of EMB in 28 patients with suspected ICIM, histopathologic grade correlated with myocardial injury as measured by troponin levels, but not with B-type natriuretic peptide levels, left ventricular ejection fraction, or myocardial necrosis and fibrosis, as evidenced by late gadolinium enhancement on cardiac MRI. There were no differences in outcomes attributable to EMB findings. The lack of concordance between the clinical workup and EMB findings is at least partially attributable to patient factors, such as time to presentation, and technical factors, such as sampling error. Overall, these findings preclude the routine use of EMB in suspected ICIM.

Given the lack of pathognomonic signs, the diagnosis of ICIM remains one of exclusion and relies on a comprehensive clinical assessment. Secondary causes of myocardial injury, such as acute myocardial infarction, should be ruled out. The co-occurrence of myocardial injury with other irAEs, such as myositis or myasthenia gravis, and severity of the illness at presentation support the initiation of high-dose steroids early in the disease course while additional workup occurs. EMB should be considered in select patients when secondary causes of myocardial injury cannot be ruled out and the risks of immunosuppression may outweigh the benefits.

Kidney

Renal irAEs are much less common; current reports estimate an overall incidence of approximately 2.2%, with grade 3/4 toxicities in <1%. The median time to renal irAEs was 91 days in this series, with a range of 21 to 245 days. Renal irAE incidence was as high as 4.9% for ipilimumab in combination with nivolumab compared with 1.4% to 2% for single-agent ICI. The most common presentation includes an elevated creatinine level, sterile mild pyuria and/or subnephrotic-range proteinuria, and minimal if any electrolyte abnormalities (ie, renal tubular acidosis). Patients are rarely symptomatic; however, some may present with fever. Other more common causes of renal dysfunction, such as dehydration or exposure to nephrotoxins like nonsteroidal anti-inflammatory drugs, contrast agents, bisphosphonates, and proton pump inhibitors, can confound assessment. Concomitant cytotoxic chemotherapies and targeted therapies can also contribute to toxicities and diagnostic uncertainty.

Pathologically, acute interstitial nephritis (AIN) is the most common manifestation. In one series of 13 patients who had renal biopsies, pathologic analysis showed AIN in 12 patients, and 3 had granulomatous features. The last patient had thrombotic microangiopathy (TMA) without evidence of AIN. Most patients treated with glucocorticoids demonstrated a partial or complete recovery; however, 2 patients with AIN not treated with glucocorticoids and the patient with TMA who received glucocorticoids did not recover renal function.

Other less common pathologic findings include acute tubular injury, pauci-immune glomerulonephritis, IgA nephropathy, focal segmental glomerulosclerosis, C3 glomerulonephropathy, lupus nephropathy, membranous nephropathy, TMA, and vasculitis. In a single-institution study, 16 patients with biopsies performed for suspected renal irAE were identified over a 10-year period. Biopsies were notable for tubulointerstitial inflammation in 14; 5 had only AIN with eosinophilic infiltrates. Glomerulonephropathies were present in 9 of the 16 patients. Another patient developed nephrotic range proteinuria in the absence of hematuria, pyuria, or change in estimated glomerular filtration rate and was found to have early membranous glomerulonephritis with CD3+, CD4+, and CD8+ T cells present.

A multicenter retrospective study was recently reported for 138 patients with ICI-induced acute kidney injury, defined as acute kidney injury attributed to ICIs and at least a doubling of baseline creatinine or requirement for renal replacement therapy. Sixty patients had biopsies, with AIN pathologically diagnosed in 93%. The other 4 biopsies showed minimal-change disease with acute tubular injury, ANCA-negative pauci-immune crescentic glomerulonephritis, anti-glomerular basement membrane disease, and C3 glomerulonephritis. Treatment with glucocorticoids was associated with a greater odds of complete kidney recovery. Among patients with...
biopsy-confirmed AIN, no histologic feature was associated with kidney recovery.

Given the high chance of non-irAE causes of renal dysfunction and sometimes bland clinical presentations, a renal biopsy may be considered for any-grade renal toxicity. An analysis of risks and benefits is critical, wherein bleeding risk and solitary kidney status would be important considerations. Renal biopsies typically are performed or coordinated by nephrology, thus consultation with a nephrologist is recommended (Table 1). The role of biopsy is supported by several groups.41-44-46 A biopsy may be pursued early to establish a diagnosis, depending on the clinical presentation, and may be useful when other cancer agents are used in combination with ICIs.49 Empirical steroids should be decided based on the severity of the patient's presentation, differential diagnosis, and risk of waiting to start steroids, and the rapidity of obtaining the biopsy. If steroid treatment is indicated for another irAE, it may be reasonable to proceed with steroids and continue to evaluate. If not performed at the outset, a biopsy should be considered if limited or no improvement is seen with steroid treatment. It should be noted that creatinine levels typically improve with steroid treatment in renal irAEs, but do not always return to baseline. Steroid treatment can impact pathology results, and therefore discussion with a pathologist is often valuable. Biopsy results, such as evidence of vasculitis or TMA, may have implications for management and ICI rechallenge.

Conclusions

Treatment with ICIs is an integral part of oncology, and is impacting subspecialty care as well. Given the myriad presentations of irAEs and variations in management, biopsies may guide important aspects of care, such as supporting or rejecting an ICI diagnosis, determining severity of the ICI, or assessing for cancer progression. This information may assist in the dosing/tapering of steroids and ICI rechallenge decisions. The potential benefits of a biopsy need to be weighed against the potential risk for each patient. As we advance our understanding of these agents and host immune systems, we will continue to evolve the use of ICIs to optimize their efficacy and minimize and manage toxicity. Pathologic specimens will continue to play an important role in elucidating the mechanisms of anticancer activity and of immune toxicities from ICIs, with the goal of the best possible patient outcomes.

References


38. Champion SN, Stone JR. Immune checkpoint inhibitor associated myocarditis occurs in both high-grade and low-grade forms. Mod Pathol 2020;33:99–108.


