

Checkpoint Inhibitors for Those with Complex Medical Needs

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Immune checkpoint inhibitors have been approved by the FDA for multiple cancer types. As approvals have expanded, so has access to these agents for patients who would not have been eligible to receive them on a clinical trial. Patients with complex medical needs, such as those with active autoimmune conditions, hepatitis B or C, and those receiving corticosteroids at baseline, may now receive these agents in the community. This raises important questions regarding safety, monitoring, and the likelihood of an anticancer response in these patients. I would like to highlight key data that provides guidance in these situations.

How are you mitigating risk for your patients with complex medical needs prior to beginning immunotherapy?

In a study of 56 non-small cell lung cancer (NSCLC) patients with autoimmune conditions treated with anti-PD-1, 26% developed a high-grade immune toxicity and 13% had a high-grade flare of their known condition. However, these patients still sustained a response to therapy comparable to those without autoimmune conditions (22%, mainly second-line NSCLC). Patients who were symptomatic from their autoimmune condition to start with had a greater chance of a flare of the autoimmune condition.

In a phase I/II trial (CheckMate 040), nivolumab was administered to patients with advanced hepatocellular carcinoma with and without hepatitis B (HBV) or C (HCV). Patients had Child-Pugh scores of <7 (dose-escalation) and <6 (dose-expansion). Patients with HBV infection received antiviral therapy (viral load <100 IU/mL), which was not required for patients with HCV infection. Toxicity profiles were similar and acceptable in both infected and noninfected groups, and both groups responded to therapy. Anti-PD-1 displayed limited

antiviral activity, with some changes in HCV RNA, and no cases of hepatitis B reactivation or anti-HBs seroconversion.

Another study showed that in 640 NSCLC patients treated with anti-PD-1/L1, 88 patients received baseline steroids \geq 10mg/day prednisone or equivalent. Progression-free survival and overall survival were poorer in those receiving baseline steroids versus those receiving no steroids or <10mg/day prednisone or equivalent.

With this data in mind, I would caution these patients that their risk of immune-related toxicity may be higher than those reported in clinical trials. In patients with active autoimmune conditions I often ask the patient's relevant medical subspecialist for a reassessment prior to starting immunotherapy and to consider the role of pretreatment if a patient is symptomatic from their condition (supportive care or prednisone <10mg/day, as allowed in clinical trials).

In patients with HBV or HCV, I would consult a hepatologist prior to treatment, assess a Childs-Pugh score, and would consider therapy if they meet the criteria used in CheckMate040. For patients already receiving corticosteroids at a dose \geq 10mg/day of prednisone/ equivalent, it may be prudent to reduce this to <10mg/day prior to the start of treatment, if clinically appropriate.

These patients may be monitored more often to identify an immune-related adverse event early, by weekly visits or provider phone calls, however immune-related toxicities can occur at any time during and even after therapy.



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