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Recent Guidelines Updates: Implications to Practice

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Mukherjee:
This is CME on ReachMD, and I'm Dr. Sudipto Mukherjee. Today, I'm reviewing the recent guideline updates in Castleman disease and the implications for your clinical practice. The National Comprehensive Cancer Network, or NCCN, in 2024 revised and updated the guidelines for idiopathic multicentric Castleman disease, or iMCD. According to the revised guidelines, all patients diagnosed with iMCD who have active disease at the time of presentation but no organ failure, the preferred first-line agent for treatment is siltuximab. And these patients, once they're started on siltuximab and they respond to siltuximab, the treatment should be continued indefinitely until disease progression or unacceptable toxicities.

Now, iMCD is a non-neoplastic lymphoproliferative disorder characterized by chronic inflammation, primarily driven by cytokines. In iMCD patients there is high levels of circulating cytokines, and one of the principal drivers of iMCD pathogenesis and clinical manifestation is interleukin 6. Siltuximab is a monoclonal antibody that binds to soluble and membrane-bound interleukin 6, thereby inhibiting the binding of this interleukin 6 to IL-6 receptors and, therefore, mitigating the downstream complications.

These findings have big implications for the clinical practice. iMCD patients, as we know, are very symptomatic at the time of diagnosis with an average of 7 or 8 symptoms. They can have a total of 27 unique symptoms. One of the primary goals of managing patients with iMCD is symptom alleviation and preventing serious complications using interleukin 6 inhibitors. This is where siltuximab fits the role.

Population-level studies in the US have shown that iMCD patients who are not treated in a timely manner or are kept under wait-and-watch can develop a variety of complications including blood clots, organ failure, particularly respiratory and renal, and can have a host of other unrelated cancers. The exact biological connection is still not clearly understood. However, we know from studies that have been done in long-term siltuximab users, that these adverse events have not been reported, suggesting that siltuximab might have a disease-modifying effect.

Moreover, according to the NCCN Guidelines, iMCD patients with active disease should be eligible for siltuximab therapy. And in fact, most of the patients that we see in clinical practice with iMCD will have active disease at presentation.

Active disease typically means these patients have fevers, they have elevated C-reactive protein, which is an inflammatory marker, and they need to have any 3 out of the 12 clinical or lab features. All these are very easy to find in iMCD patients. Essentially, what these guidelines suggest is that any iMCD patient at the time of diagnosis, knowing that they would have some level of active disease at the time of diagnosis, should be promptly treated with siltuximab and the treatment should be continued as long as the patients are responding to the treatment, until there is evidence of disease progression or unacceptable toxicity.

Thanks for tuning in for this brief discussion. I hope you will find it useful in your practice.

Announcer:
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