

MCLs with a mutation in *TP53* or a complex karyotype are particularly high risk as well. Over two-thirds of patients will have stage IV disease, mostly with bone marrow and peripheral blood involvement, at the time of diagnosis. Another common extranodal site of involvement is the gastrointestinal tract, where diffuse lymphomatous polyposis may be seen.

The pathognomonic cytogenetic finding in MCL is t(11;14), which brings the gene for the cell cycle control protein cyclin D1 under the control of the immunoglobulin heavy chain gene promoter on chromosome 14. This translocation is present in >90% of cases. The remaining cases usually overexpress cyclin D2, cyclin D3, or cyclin E. Tumor cells also are positive for B cell markers CD19 and CD20, as well as CD5. They usually lack CD10 and CD23.

Therapies for MCL are evolving. Patients with localized disease might be treated with combination chemotherapy followed by radiotherapy; however, these patients are exceedingly rare. Similarly, patients with the indolent variant can be observed until disease progresses to cause symptoms or signs of organ function impairment. For the usual presentation with disseminated disease, standard lymphoma treatments like R-CHOP have been unsatisfactory, with the minority of patients achieving complete remission. The addition of high-dose cytarabine to an R-CHOP-like backbone with or without consolidation autologous stem cell transplantation in first remission has improved progression-free survival, but it has not elicited cures in this disease. These include the Nordic regimens and R-HyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, dexamethasone, cytarabine, and methotrexate). BR has activity in this disease and is more effective and better tolerated than R-CHOP. Newer studies with short follow-up suggest that strategies that combine BR with cytarabine with or without autologous stem cell transplant may be effective and well tolerated. Maintenance rituximab, following a good response to induction chemotherapy or after autologous stem cell transplant, also improves outcomes over observation alone. For relapsed disease, the BTK inhibitors ibrutinib and acalabrutinib have single-agent activity with a response rate of almost 70% but a response duration of only 18 months. These drugs are being