A high TP53 mutation burden is a strong predictor of primary refractory mantle cell lymphoma.

**Abstract**

Survival for patients with mantle cell lymphoma has improved dramatically over the last 2 decades owing to a better understanding of disease biology and the development of more effective treatment regimens for patients with untreated and relapsed disease. With these advancements, we are now poised to ask questions that challenge old treatment strategies, use new technologies, and improve our understanding of disease heterogeneity. This article focuses on questions that we believe will drive the future of mantle cell lymphoma treatment. Although not an exhaustive list, we review current literature, ongoing studies, and provide expert opinion on future trial design.

**PMID: 32861291 [PubMed — as supplied by publisher]**

**Understanding Health-Related Quality of Life in Patients with Mantle Cell Lymphoma.**

**Abstract**

Mantle cell lymphoma (MCL) is a unique lymphoma that is heterogeneous in its clinical course, and lacks consensus treatment approaches. It is often treated with immunochemotherapy at diagnosis and chronic therapies in relapse. Despite significant advances in therapy, MCL remains incurable. Maintaining patients’ health-related quality of life (HRQOL) is an important treatment goal. Assessment of HRQOL elucidates the impact of an illness and its treatment on patients’ lives. This review highlights the relevance of HRQOL assessment in MCL, evaluates existing evidence, current knowledge gaps and challenges in HRQOL assessment, and defines future directions for improving HRQOL evaluation in MCL patients.

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Allogeneic Transplantation and Chimeric Antigen Receptor-Engineered T-Cell Therapy for Relapsed or Refractory Mantle Cell Lymphoma.

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Allogeneic Transplantation and Chimeric Antigen Receptor-Engineered T-Cell Therapy for Relapsed or Refractory Mantle Cell Lymphoma.

Authors: Gauthier J, Maloney DG
Abstract
Mantle cell lymphoma (MCL) accounts for fewer than 10% of non-Hodgkin lymphoma. There is a high initial response rate to chemotherapy and rituximab, but a nearly universal risk of relapse. Allogeneic hematopoietic cell transplantation (allo-HCT) provides one of the only curative options. We review the role of allo-HCT for relapsed and refractory (R/R) MCL and discuss a novel promising approach using autologous chimeric antigen receptor-engineered T (CAR-T) cells. We review preliminary safety and efficacy data of 2 pivotal trials investigating the use of CD19-targeted CAR-T cells for R/R MCL after ibrutinib failure and discuss potential timing of these approaches.

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Blastoid Mantle Cell Lymphoma.

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Blastoid Mantle Cell Lymphoma.

Authors: Jain P, Wang M
Abstract
Blastoid and pleomorphic mantle cell lymphoma (MCL) are among the worst prognostic, aggressive histology, high-risk variants of MCL, and, in this article, they are presented as blastoid MCL. Blastoid MCL have not been systematically studied, probably due to their rarity. De novo blastoid MCLs have superior outcomes compared with transformed MCL. Compared with classic MCL, extranodal involvement (mainly skin, central nervous system), frequent relapses, and inferior responses to conventional chemoimmunotherapy, BTK inhibitors and venetoclax are frequent in blastoid MCL. KTE-X19 induces excellent response in blastoid MCL. Combinations with novel agents are actively investigated. This article presents a comprehensive review on blastoid MCL in 2020.

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What Causes Bruton Tyrosine Kinase Inhibitor Resistance in Mantle Cell Lymphoma and How Should We Treat Such Patients?

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What Causes Bruton Tyrosine Kinase Inhibitor Resistance in Mantle Cell Lymphoma and How Should We Treat Such Patients?

Authors: McCulloch R, Eyre TA, Rule S
Abstract
In this review, we explore insights into the pathophysiology of Bruton tyrosine kinase inhibitor (BTKi) resistance in mantle cell lymphoma, and consider potential therapeutic targets. We review the possible clinical benefits of giving BTKIs alongside other novel therapies, and evaluate clinical data for treatment strategies post BTKi progression that may help guide current practice. We conclude by considering future approaches, including the potential role of chimeric antigen receptor T-cell therapy.

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Current Role and Emerging Evidence for Bruton Tyrosine Kinase Inhibitors in the Treatment of Mantle Cell Lymphoma.

Related Articles

Current Role and Emerging Evidence for Bruton Tyrosine Kinase Inhibitors in the Treatment of Mantle Cell Lymphoma.

Authors: Bond DA, Maddocks KJ
Abstract
The Bruton tyrosine kinase inhibitors (BTKi), acalabrutinib, ibrutinib, and zanubrutinib, are all approved in the United States for the treatment of relapsed mantle cell lymphoma (MCL). BTKi as a class have become the preferred therapy for most of the patients with relapsed MCL, and ongoing clinical trials are evaluating whether combining BTKi with other targeted agents may deepen response and further improve outcomes. Emerging evidence supports the efficacy of BTKi-containing combinations as frontline treatment, and clinical studies to define the role of this class of drugs for newly diagnosed patients with MCL are in progress.

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Minimal Residual Disease in Mantle Cell Lymphoma: Methods and Clinical Significance.

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Minimal Residual Disease in Mantle Cell Lymphoma: Methods and Clinical Significance.
Authors: Ladetto M, Tavarozzi R, Pott C

Abstract
Several biological and clinical features have been recognized in mantle cell lymphoma (MCL). In recent years, the minimal residual disease (MRD) has been extensively investigated and is now considered as one of the strongest clinical predictors in this lymphoma. This article reviews methods used for the assessment of MRD in MCL and discusses their strengths and weaknesses. In addition, it examines the MRD contribution to the biology knowledge of MCL and the development of effective strategies for its management, including the possibility of personalized treatment based on MRD response.

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Approach to the Initial Treatment of Older Patients with Mantle Cell Lymphoma.

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Approach to the Initial Treatment of Older Patients with Mantle Cell Lymphoma.
Authors: Ruan J

Abstract
With a median age of 65 years, mantle cell lymphoma affects predominantly older patients with comorbidities. Initial treatment of older patients is not standardized but traditionally includes chemoimmunotherapy regimens that are not curative. Incorporation of maintenance strategy after induction and introduction of novel agents have expanded access to effective treatment options and improved survival outcome. Ongoing randomized studies comparing induction regimens and maintenance strategies are expected to further define the role of novel agents and combinations in the initial treatment of older patients with mantle cell lymphoma.

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Initial and Consolidation Therapy for Younger Patients with Mantle Cell Lymphoma.

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Initial and Consolidation Therapy for Younger Patients with Mantle Cell Lymphoma.
Authors: Guy D, Kahl BS

Abstract
Mantle cell lymphoma is an incurable B-cell malignancy. Treatment of young fit patients is particularly challenging, because careful consideration should be made when building a long-term treatment strategy that would provide longer remissions and increase patients’ quality of life. Most young fit patients achieve long remissions with a combination of immunchemotherapy containing rituximab and high-dose cytarabine, followed by high-dose chemotherapy and autologous stem-cell transplantation. The addition of maintenance therapy with rituximab following autologous stem-cell transplantation prolongs the time to relapse and increases overall survival. Despite an intensive approach, late relapses are common and are usually treated with novel agents.

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Is Limited-Stage Mantle Cell Lymphoma Curable and How Is It Best Managed?

Related Articles

Is Limited-Stage Mantle Cell Lymphoma Curable and How Is It Best Managed?
Authors: Romancik JT, Cohen JB

Abstract
Limited-stage (stage I-II) mantle cell lymphoma (MCL) is rarely encountered. There is no standard approach to treatment and available data to guide management decisions mainly are retrospective studies. A thorough staging evaluation, including positron emission tomography/computed tomography, bone marrow biopsy, and gastrointestinal evaluation, should be completed because disseminated disease is common. Radiation therapy is effective for local control, and, although prolonged remission can be achieved, distant relapses are common and there are insufficient data to say that patients can be cured using this treatment. This article reviews literature pertaining to management of patients with limited-stage MCL and discusses approach to treatment.

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Watch and Wait in Mantle Cell Lymphoma.

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**Watch and Wait in Mantle Cell Lymphoma.**


Authors: Lee C, Martin P

Abstract

Mantle cell lymphoma (MCL) is a biologically heterogeneous disease, and patients may experience a clinical course ranging from indolent to very aggressive. Observational studies suggest that a subset of patients can be safely observed for a period of months to years from initial diagnosis without adversely impacting their outcomes. However, identification of candidates for the "watch and wait" approach remains challenging because selection criteria are not well-defined. Studies that prospectively stratify patients on the basis of MCL biology and disease risk will be informative, and patients with indolent MCL may be ideal candidates for frontline clinical trials exploring novel therapies.

PMID: 32861281 [PubMed — as supplied by publisher]

What Is Responsible for Heterogeneity in Mantle Cell Lymphoma Biology and Outcomes?

Related Articles

**What Is Responsible for Heterogeneity in Mantle Cell Lymphoma Biology and Outcomes?**


Authors: Witzig TE

Abstract

Mantle cell lymphoma, despite its common derivation from a t(11;14) error that occurs in a naïve B-cell leading to overexpression of cyclin D1 protein, is characterized by substantial heterogeneity in biology and clinical outcome. Unlike other non-Hodgkin lymphoma types, it is more common in men. Clinical presentation patterns vary from nodal to splenomegaly with leukemia to gastrointestinal involvement. Biological variability is linked to tumor cell proliferation. Increased monocyte/macrophages and their associated proinflammatory cytokines are associated with inferior outcomes. These clues mandate that new treatments should target signal pathways that contribute to these adverse outcomes.

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Cell Cycle Dysregulation in Mantle Cell Lymphoma: Genomics and Therapy.

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**Cell Cycle Dysregulation in Mantle Cell Lymphoma: Genomics and Therapy.**


Authors: Wang K, Huang X, Di Liberto M, Chen-Kiang S

Abstract

Cell cycle dysregulation caused by aberrant cyclin D1 and CDK4 expression is a major determinant for proliferation of cancer cells in mantle cell lymphoma (MCL). Inhibition of CDK4/6 induces G1 arrest of MCL cells in patients, appearing to deepen and prolong the clinical response to partner agents. This article reviews aberrations of cell cycle genes in MCL cells and clinical trials of CDK4/6 inhibitors for MCL. Integrative longitudinal functional genomics is discussed as a strategy to discover genomic drivers for resistance in cancer cells and cancer-immune interactions that potentially contribute to the clinical response to palbociclib combination therapy in MCL.

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Molecular Pathogenesis of Mantle Cell Lymphoma.

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**Molecular Pathogenesis of Mantle Cell Lymphoma.**


Authors: Navarro A, Beà S, Jares P, Campo E

Abstract

Mantle cell lymphoma (MCL) is a mature B-cell neoplasm with heterogeneous clinical behavior molecularly characterized by the constitutive overexpression of cyclin D1 and deregulation of different signaling pathways. SOX11 expression determines an aggressive phenotype associated with accumulation of many chromosomal alterations and somatic gene mutations. A subset of patients with the SOX11-negative leukemic non-nodal MCL subtype follows an initial indolent clinical evolution and may not require treatment at diagnosis, although eventually may progress to an aggressive disease. We discuss the genetic and molecular alterations with impact on the cancer hallmarks that characterize the lymphomagenesis of the 2 MCL subtypes.

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