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Hodgkin's Lymphoma: Biology and Treatment Strategies for Primary, Refractory, and Relapsed Disease

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Abstract

Hodgkin's lymphomas belong to the most curable tumor diseases in adults. About 80% of patients in all anatomical stages and of all histological subtypes can be cured with modern treatment strategies. In spite of the great clinical progress, the pathogenesis of this peculiar lymphoproliferative entity has not been elucidated completely up until now.

In Section I Drs. Stein, Hummel, and Zollinger describe the different pro-proliferative and antiapoptotic pathways and molecules involved in the transformation of the germinal center B-lymphocyte to the malignant Hodgkin-Reed-Sternberg cell. They use a comprehensive gene expression profiling (Affymetrix gene chip U133A) on B- and T-Hodgkin cell lines and state that the cell of origin is not the dominant determinant of the Hodgkin cell phenotype, but the transforming event. H-RS cells lack specific functional markers (B-T-cell receptors) and physiologically should undergo apoptosis. Why they do not is unclear and a matter of intensive ongoing research.

In Section II Dr. Diehl summarizes the commonly used primary treatment strategies adapted to prognostic strata in early, intermediate and advanced anatomical stages using increasing intensities of chemotherapy (two, four, eight courses of chemotherapy such as ABVD) and additive radiation with decreased doses and field size. ABVD is without doubt the gold standard for early and intermediate stages, but its role as the standard regimen for advanced stages is challenged by recent data with time- and dose-intensified regimens such as the escalated BEACOPP, demonstrating superiority over COPP/ABVD (equivalent to ABVD) for FFTF and OS in all risk strata according to the International Prognostic Score.

In Section III, Dr. Connors states that fortunately there is a considerably decreased need for salvage strategies in Hodgkin's lymphomas since primary treatment results in a more than 80% tumor control. Nevertheless, a significant number of patients experience either a tumor refractory to therapy or an early or late relapse. Therefore, one of the continuing challenges in the care for Hodgkin's lymphomas today is to find effective modes for a second tumor control. High-dose chemotherapy followed by autologous stem cell support has proved to be the treatment of choice when disseminated tumors recur after primary chemo- and or radiotherapy. Nodal relapses respond well to local radiation when they recur outfield of primary radiation without B-symptoms and in stages I–II at relapse. Allogeneic stem cell support needs further intensive evaluation in controlled studies to become an established alternative.

Topics: bleomycin/dacarbazine/doxorubicin/vinblastine protocol, chemotherapy regimen, hodgkin's disease, radiation therapy

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• Primary Treatment of Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL): CS IA-IVB (HODG-13). Follow-up After Completion of Treatment and Monitoring for Late Effects (HODG-14) Refractory CHL (HODG-15) Suspected Relapse of CHL (HODG-16) Refractory or Suspected Relapse of NLPHL (HODG-17) Unfavorable Risk Factors for Stage I-II CHL (HODG-A) Principles of Systemic Therapy (HODG-B) Principles of Radiation Therapy (HODG-C) PET 5-Point Scale (Deauville Criteria) (HODG-D) Principles of Systemic Therapy for Relapsed or Refractory Disease (HODG-E) Management of CHL in Older Adults (HODG-F) Staging (ST-1). Clinical Trials: NCCN believes that the best management for any patient with cancer is in a clinical trial. Hodgkin lymphoma (HL) is a malignant lymphoma that is typically of B-cell origin. The incidence of HL has a bimodal age distribution, with peaks in the 3rd and... Primary refractory or relapsed disease: trial of alternative chemotherapy or consideration of high-dose chemotherapy and autologous stem cell transplantation. Independent of stage, treatment is typically initiated with curative intent! References:[9]. Initial evaluation and diagnosis of classical Hodgkin lymphoma in adults. In: Post TW, ed. UpToDate. Waltham, MA: UpToDate. <https://www.uptodate.com/contents/initial-evaluation-and-diagnosis-of-classical-hodgkin-lymphoma-in-adults>. Last updated March 9, 2015. Accessed March 19, 2017. 8. Mauch PM, Canellos GP, Arnold S, Freedman AS, Rosmarin AG. NCCN Hodgkin Lymphoma Panel Members Summary of Guidelines Updates Diagnosis and Workup (HODG-1) Primary Treatment. • Classical Hodgkin Lymphoma: CS IA-IIA Favorable (HODG-2) CS I-II Unfavorable (Bulky disease) (HODG-4) CS I-II Unfavorable (Non-bulky disease) (HODG-8) CS III-IV (HODG-9). • Nodular Lymphocyte-Predominant Hodgkin Lymphoma: CS IA-IVB (HODG-12). Follow-up After Completion of Treatment and Monitoring For Late Effects (HODG-13) Refractory Classical Hodgkin Lymphoma (HODG-14). Clinical Trials: NCCN believes that the best management for any cancer patient is in a clinical trial. Partic The most effective salvage strategy for patients with Hodgkin's lymphoma relapsed or refractory to front-line therapy has yet to be conclusively defined. This problem has evolved in the last years and it is time to reconsider its dimension and to comment on mature data, new facts and perspectives. One of the most important new facts is the introduction of fluorodeoxyglucose positron emission tomography (FDG-PET) evaluation of response during the induction treatment. About 20–25% of patients with advanced Hodgkin's disease do not achieve a complete remission (primary resistant disease) with the standard front-line ABVD chemotherapy or the alternating ABVD and MOPP regimens, and a proportion of remitters will relapse at different time intervals (relapsed disease).