Strategies To Overcome Myelotoxic Therapy For The Treatment Of Burkitt's And Aids-related Non-hodgkin's Lymphoma

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Abstract:

Department of Microbiology and Immunology, SUNY Upstate Medical University, Syracuse, NY 13210, USA. BACKGROUND: Strategies to circumvent or lessen the myelotoxicity associated with combination chemotherapy may improve the overall outcome of the management of patients particularly in resource poor settings. OBJECTIVES: To develop effective non-myelotoxic therapies for Burkitt's Lymphoma (BL) and AIDS-related non-Hodgkin's lymphoma. DATA SOURCES: Publications, original and review articles, conference abstracts searched mainly on Pubmed indexed for medline. DATA EXTRACTION: A systematic review of the clinical problem of combination chemotherapy. Identification of clinical strategies that circumvent or lessen the myelotoxicity of combination cytotoxic chemotherapy. Length of survival, lack of clinically significant (> grade 3) myelosuppression and weight loss were used as markers of myelotoxicity. DATA SYNTHESIS: Review of published experience with some of these strategies including dose-modification of multi-agent chemotherapy; rationale for targeted therapies, and the preclinical development of a mouse model exploring the role of metronomic scheduling substantiate pragmatism and feasibility of these approaches. CONCLUSION: Myelotoxic death rates using multi-agent induction chemotherapy approach 25% for endemic Burkitt's lymphoma and range between 20% to 60% for AIDS-related malignancy. This is mostly explained by the paucity of supportive care compounded by wasting and inanition attributable to advanced cancer and HIV infection making patients more susceptible to myelosuppressive side effects of cytotoxic chemotherapy. Investigations and alternative approaches that lessen or circumvent myelotoxicity of traditional cytotoxic chemotherapy for the management of Burkitt's lymphoma and AIDS-related non-Hodgkin's lymphoma in the resource-constrained setting are warranted. Pertinent pre-clinical and clinical data are emerging to support the need for abrograting the myelosuppressive effects of traditional cytotoxic chemotherapy. This can be achieved by developing targeted anti-viral and other strategies, such as the use of bryostatin 1 and vincristine, and by developing a preclinical mouse model to frame the clinical rationale for a pilot trial of metronomic therapy for the treatment of Burkitt's and AIDS-related lymphoma. Implementation of these investigational approaches must be encouraged as viable anti-cancer therapeutic strategies particularly in the resource-constrained settings.