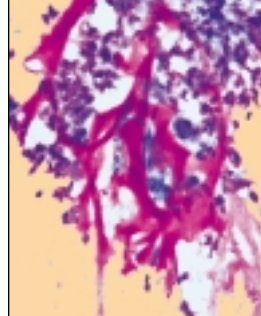


TEN BEST READINGS ON HEMATOLOGIC MALIGNANCIES

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Grillo-Lopez AJ. Rituximab: an insider's historical perspective. *Semin Oncol.* 2000;27:9-16.

Rituximab is the first therapeutic monoclonal antibody approved specifically for therapy for lymphoma. Substantial research has been performed to further the understanding of this novel agent. Nevertheless, work is still needed on mechanism of action and resistance, combinations with chemotherapy, biologics and radiotherapy/radioimmunotherapy, its role within multimodality regimens, and nonmalignant applications.

Davis TA, Grillo-Lopez AJ, White CA, et al. Rituximab anti-CD20 monoclonal antibody therapy in non-Hodgkin's lymphoma: safety and efficacy of re-treatment. *J Clin Oncol.* 2000;18:3135-3143.

The overall response rate in 57 assessable patients was 40% (11% complete response rate and 30% partial response rate). Median time to progression in responders and median duration of response have not been reached, but Kaplan-Meier estimated medians are 17.8 months and 16.3 months, respectively. These estimated medians are longer than the medians achieved in the patients' prior course of rituximab. In this re-treatment population, safety and efficacy were not apparently different from those after initial rituximab exposure.

McDevitt MR, Ma D, Lai LT, et al. Tumor therapy with targeted atomic nanogenerators. *Science.* 2001;294:1537-1540.

The authors have developed methods to target molecular-sized

generators of alpha-emitting isotope cascades to the inside of cancer cells using actinium-225 coupled to internalizing monoclonal antibodies. In vitro, these constructs specifically killed leukemia, lymphoma, breast, ovarian, neuroblastoma, and prostate cancer cells at becquerel (picocurie) levels.

Press OW, Eary JF, Gooley T, et al. A phase I/II trial of iodine-131-tositumomab (anti-CD20), etoposide, cyclophosphamide, and autologous stem cell transplantation for relapsed B-cell lymphomas. *Blood.* 2000;96:2934-2942.

The maximum tolerated dose of ¹³¹I-tositumomab that could be safely combined with 60 mg/kg of etoposide and 100 mg/kg of cyclophosphamide delivered 25 Gy to critical normal organs. The estimated overall survival and progression-free survival of all treated patients at 2 years was 83% and 68%, respectively.

Fontaine P, Roy-Proulx G, Knafo L, et al. Adoptive transfer of minor histocompatibility antigen-specific T lymphocytes eradicates leukemia cells without causing graft-versus-host disease. *Nat Med.* 2001;7:789-794.

The critical issue of a possible dissociation of the antileukemic effect and graft-vs-host disease by targeting specific minor histocompatibility antigens remains unresolved. The authors show that effective and nontoxic immunotherapy of hematologic malignancies can be achieved by targeting a single immunodominant minor histocompatibility antigen.

The 10 best recent articles in the medical literature relating to immunotherapy of hematologic malignancies are reviewed here.

Ten Best Readings

Dazzi F, Szydlo RM, Craddock C, et al. Comparison of single-dose and escalating-dose regimens of donor lymphocyte infusion for relapse after allografting for chronic myeloid leukemia. *Blood*. 2000;95:67-71.

The incidence and severity of acute and chronic graft-vs-host disease (GVHD) were both significantly lower for recipients treated by escalating dose regimen than for recipients treated by bulk dose regimen. These findings suggest that the incidence of GVHD associated with an escalating dose regimen is low, not because the final cell dose is small, but because lymphocytes are administered over a considerable number of months.

Timmerman JM, Levy R. The history of the development of vaccines for the treatment of lymphoma. *Clin Lymphoma*. 2000;1:129-139.

Vaccination with tumor-specific immunoglobulin or idiotype (Id) is a promising new form of immunotherapy for B-cell malignancies. Id protein vaccination has demonstrated clinical activity in B-cell lymphomas, yet it requires the laborious and time-consuming procedures of tumor-myeloma cell hybridization, large-scale in vitro culture, and protein purification. Recombinant adenoviruses are highly efficient and immunogenic gene transfer vehicles from which individualized vaccines can be rapidly assembled using polymerase chain reaction-amplified tumor Id genes.

Pinilla-Ibarz J, Cathcart K, Korontsvit T, et al. Vaccination of

patients with chronic myelogenous leukemia with bcr-abl oncogene breakpoint fusion peptides generates specific immune responses. *Blood*. 2000;95:1781-1787.

A tumor-specific bcr-abl-derived peptide vaccine can be safely administered to patients with chronic-phase CML and can elicit a bcr-abl peptide-specific immune response despite the presence of active disease in these patients.

Clark RE, Dodi IA, Hill SC, et al. Direct evidence that leukemic cells present HLA-associated immunogenic peptides derived from the Bcr-Abl b3a2 fusion protein. *Blood*. 2001;98:2887-2893.

These patients mounted a cytotoxic T-lymphocyte response to KQSSKALQR that also killed autologous chronic myeloid leukemia (CML) cells, and tetramer staining demonstrated the presence of circulating KQSSKALQR-specific T cells. The findings are the first demonstration that CML cells express HLA-associated leukemia-specific immunogenic peptides and provide a sound basis for immunization studies against Bcr-Abl.

Ghetie MA, Bright H, Vitetta ES. Homodimers but not monomers of Rituxan (chimeric anti-CD20) induce apoptosis in human B-lymphoma cells and synergize with a chemotherapeutic agent and an immunotoxin. *Blood*. 2001;97:1392-1398.

Homodimers, but not monomers, of rituximab (Rituxan) induced both apoptosis and necrosis of several B-cell lymphoma lines in vitro. The inhibition of cell growth was not dependent on the presence

of Fc receptors or on 10-fold or greater differences in the density of CD20 on the target cells. Compared with monomers, rituximab homodimers also rendered drug-resistant CD20(+) B-lymphoma cells more sensitive to chemotherapeutic agents and synergized with an anti-CD22 immunotoxin in vitro.