

Treatment of Relapsed Non-Hodgkin's Lymphoma of Childhood

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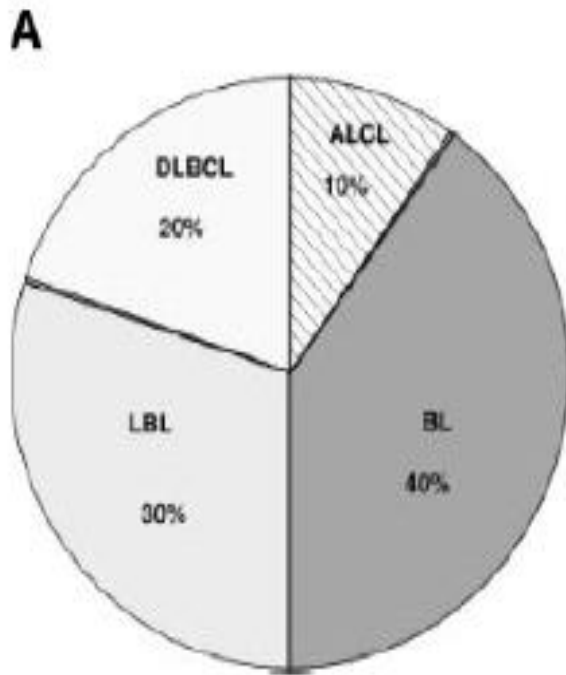
LOMBARDI CANCER CENTER

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WASHINGTON DC, USA

Distribution of Childhood NHL

Cairo et al.



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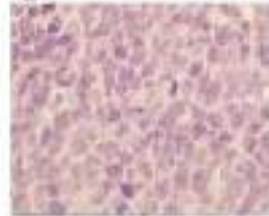
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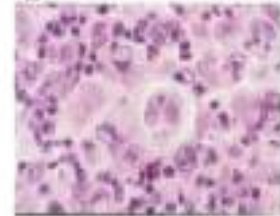
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Childhood NHL

- B-cell lymphoma
 - Burkitt's and Burkitt-like lymphoma
 - DLBCL
 - Mediastinal B-cell lymphoma
- Lymphoblastic Lymphoma
- Anaplastic Large cell lymphoma
- PTLD
- HIV Lymphoma

B-Cell NHL in Children

- B-cell lymphomas make up 6% of all NHL in children and adolescents
- 2/3 have Burkitt or Burkitt-like histology
- 1/3 have a diffuse large B-cell lymphoma (DLBCL)
- 25% patients have localized disease
- 75% have advanced disease
- 5 year EFS for limited disease is 90 -99%
- 4 year EFS for advanced disease is 60 -90%
- Mediastinal B-cell lymphoma and combined BM and CNS disease have a 4 year EFS of 60%
- Recurrent B-cell lymphoma has a 10 -30% EFS

Current Treatment for relapsed B-cell NHL

- There is no current standard treatment option for recurrent B-cell lymphoma
- Standard Treatment Options
 - Allogeneic or autologous bone marrow transplantation.
 - *DECAL*: dexamethasone, etoposide, cisplatin, cytarabine, and L-asparaginase.
 - *ICE*: ifosfamide, carboplatin, and etoposide.
- Treatment Options Under Clinical Evaluation
 - *ANHL0121*: Rituximab, ifosfamide, carboplatin, and etoposide (mature B-cell only).
 - 7/9 patients had an objective response
 - Were able to proceed with transplantation

Mediastinal B-Cell NHL

- In addition to standard options for relapse therapy
- Radiation?
 - Similarity to Hodgkin's disease
 - BFM data does not agree
 - Few patients – difficult to evaluate
 - Attractive target for radioimmune conjugate therapy?

Which Relapsed B-cell NHL patients will benefit from targeted therapy?

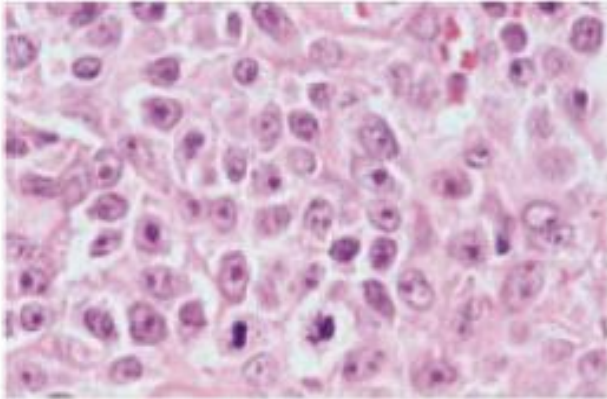
- Patients with advanced, recurrent disease or mediastinal lymphoma
 - Add targeted monoclonal antibody therapy to improve survival

Burkitt's Lymphoma

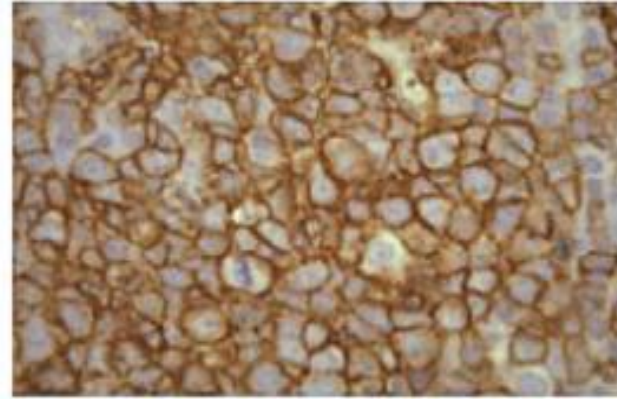
H&E

CD 20

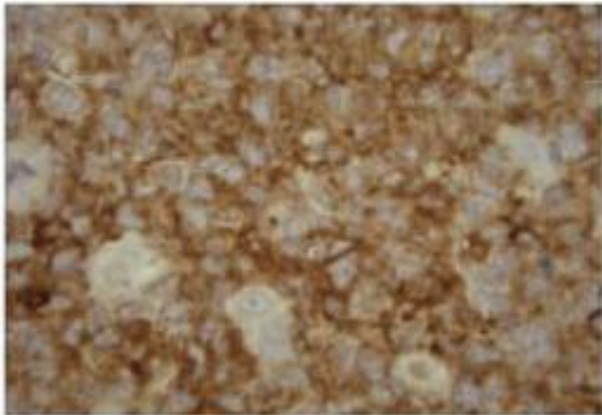
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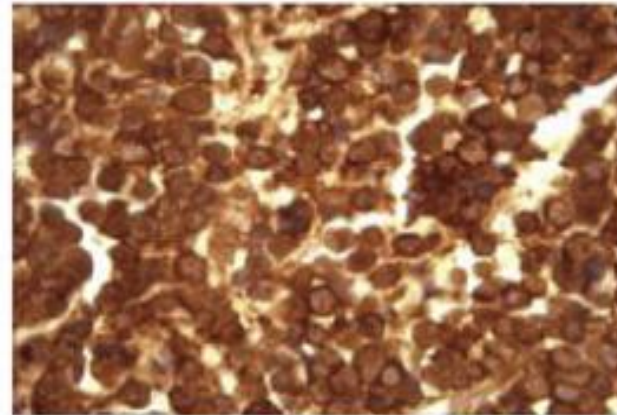
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CD 22

CD52

Monoclonal Antibody therapy for B-cell lymphoma

- Rituximab (anti CD20)
 - Naked chimeric antibody to CD20
 - Improved survival in adults with CHOP –R
 - Currently in COG trials for newly diagnosed and recurrent B-NHL
- Ibritumomab –tiuxetan Y₉₀ (anti CD20)
 - Radioimmununoconjugate antibody to CD20
 - Recently approved in adults with refractory/recurrent B-NHL
 - Currently in Phase I trials in children with refractory/recurrent B-NHL
- Epratuzumab (anti CD22)
 - > 98% B-NHL and 95% precursor-B ALL in children express CD22
 - Phase I trial with re-induction therapy for children with Precursor-B ALL
- Alemtuzumab (CD52)
 - 80% childhood Burkitt's lymphoma and 93% DLBCL express CD52
 - Phase II study as a single agent and in combination with 6MP/MTX

Lymphoblastic Lymphoma

- T-cell lymphoblastic lymphoma
 - Compound 506U78 (Nelarabine)
 - H₂O soluble prodrug of ara –G
 - Selectively toxic to T lymphoblasts
 - Single agent therapy – 1.2G/m²/day x 5 days
 - NEUROTOXICITY – BIG PROBLEM
- Currently in trial in combination with chemotherapy for upfront treatment of T-cell ALL
- Alemtuzumab (Campath 1H)
- IL-2 receptor targeted diphtheria protein (denileukin diftitox) ?
- NOTCH-1 pathway inhibitors?

Anaplastic Large-cell Lymphoma

- CD 30 + T-cell NHL
 - Primary cutaneous ALCL
 - Systemic nodal and extranodal ALCL
 - ALK expression (80-90% pediatric tumors)
- Primary cutaneous and ALK-ive ALCL rare in pediatrics
- ALK+ ALCL also express CD25 or IL-2 receptor
- Excellent results with Allogeneic BMT
 - (EFS 3 yrs around 75%)
- ICE +SGN30 (monoclonal antibody that binds to CD30)
 - ALK+ patients in 1st or 2nd relapse

PTLD and HIV lymphomas

- COG upfront study for PTLD
 - Cyclophosphamide with prednisone and rituximab
 - Relapse??
- NCI study for PTLD and HIV lymphomas
 - Cyclophosphamide, MTX, rituximab
 - Relapse – Ifosfamide, VP-16, GCSF
 - Ara-C?