

Lymphoma

Managing Older Patients

Cheryl Tompkins RN, MSN, CRNP, AOCNP
Nurse Practitioner, Stem Cell Transplant Service
University of Pittsburgh Cancer Centers
University of Pittsburgh Medical Center
Tompkinsca@upmc.edu

Overview

- Classification
- Prognosis
- Treatment
 - Focus on Follicular and Diffuse Large B-Cell NHL
- Special considerations for the management of the older patient with NHL
- Supportive Care

Non-Hodgkin's Lymphoma

- Classification based on:
 - Morphology
 - Immunophenotype
 - Genotype
 - Clinical Features

Indolent and Aggressive NHL

The Revised European/American Lymphoma – World Health Organization Classification (REAL/WHO)

■ Indolent

- **Follicular lymphoma**
- Marginal zone B-cell lymphoma, MALT type
- Marginal zone B-cell lymphoma, nodal type
- Small lymphocytic lymphoma
- Lymphoblastic lymphoma

■ Aggressive

- **Diffuse large B-cell lymphoma**
- Mantle cell lymphoma
- Peripheral T-cell lymphoma
- Primary mediastinal large B-cell lymphoma
- Anaplastic large cell lymphoma
- Lymphoblastic lymphoma
- Burkitt's-like lymphoma
- Burkitt's lymphoma

Staging

The Ann Arbor Staging System

■ Stage I

- Involves 1 lymph node or 1 organ or area outside the lymph node

■ Stage II

- >/ 2 lymph node regions on 1 side of diaphragm or 1 lymph node region + a nearby organ area

■ Stage III

- Lymph nodes on both sides of diaphragm or 1 nodal area and 1 organ on opposite sides of diaphragm

■ Stage IV

- Disease outside the lymph nodes and spleen AND spread to more than 1 organ such as bone, marrow, skin, or other

International Prognostic Index (IPI)



All Patients

- Age >60
- Serum LDH >1 x nml
- Performance Status 2-4
- Stage III or IV
- Extranodal involvement >1 site

International Index, All Pts

- | | |
|---------------------|--------|
| ■ Low | 0 or 1 |
| ■ Low/Intermediate | 2 |
| ■ High/Intermediate | 3 |
| ■ High | 4 or 5 |

Age-Adjusted IPI

Patients </ 60 yrs

- Stage III or IV
- Serum LDH >1 x normal
- Performance status 2-4

IPI Patients </ 60 yrs

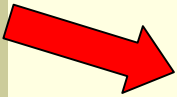
- Low 0
- Low/intermediate 1
- High/intermediate 2
- High 3

Prognosis

Follicular Lymphoma International Prognostic Index (FLIPI)

■ Factors Considered:

- Stage
 - I-II vs III-IV (negative)
- Hemoglobin
 - Greater or less (negative) than 12g/dl
- Age
 - Greater (negative) or less than 60
- Number of nodal areas
 - Greater (negative) than 4
- LDH
 - Normal or high (negative)



Prognosis

Follicular Lymphoma International Prognostic Index (FLIPI)

Risk Group	Number of factors	Distribution of Patients (%)	5-yr survival (%)	10-yr survival (%)
Low	0-1	36	90.6	70.7
Intermediate	2	37	77.6	50.9
High	>/3	27	52.5	35.5

Goal of Treatment

- Indolent Lymphoma
 - Disease control
- Aggressive Lymphoma
 - Cure

Standard Care – Follicular Lymphoma

- Stage I-II
 - Loco regional RT
 - Chemotherapy followed by RT
 - Observation

NCCN 2006

Standard Care – Follicular Lymphoma

- Stage III-IV
 - Observation
 - Local RT
 - Single agent/combination chemotherapy +/- monoclonal antibody therapy
 - Monoclonal antibody therapy
 - Intensive chemotherapy + stem cell transplant

NCCN 2006

Emerging Therapies/Questions

Follicular Lymphoma

■ Role of Rituximab

■ Rituximab added to initial chemotherapy

- CVP vs R-CVP frontline in advanced untreated FL
- Addition of rituximab to CVP improves TTP and OS Sola-Celigny et al., Abstract #350, Blood, 2005

■ “Maintenance” rituximab

- CVP+/- Maintenance rituximab in advanced indolent NHL (maintenance x 2 years)
- Resulted in significant improvement in PFS: 15 vs 61 months with no increased toxicity

Hochster et al Abstract 349, Blood 2005

■ Rituximab as “consolidation”

- Induction R-CHOP vs CHOP and maintenance rituximab vs observation in relapsed FL
- Improved OS and PFS with rituximab maintenance

Van Oers et al. Abstract 353 Blood 2005

Standard Care – Diffuse Large B-Cell NHL

- CHOP + Rituximab 6-8 cycles +/- RT
 - Considerations
 - Bulky disease
 - Prognostic factors

Diffuse Large B-Cell NHL

Management of Elderly Patient

■ Known

- R-CHOP 21 better than CHOP 21 for DLBCL in elderly (GELA trial, Coiffier NEJM 2002)
 - CR for R-CHOP 76% vs CHOP 63%, (p=0.005)
 - Addition of rituximab reduced risk of treatment failure and death
 - Clinically relevant toxicity not significantly greater with addition of rituximab
- CHOP 14 better than CHOP 21 for DLBCL in elderly (Pfreundschuh, Blood 2004)

Diffuse Large B-Cell NHL

Management of Elderly Patient

- Results from RICOVER – 60 Trial Purpose:
 - CHOP 14 vs R-CHOP 14
 - 6 vs 8 cycles
- Primary endpoint was freedom from treatment failure (FFTF)
- 1330 patients
- Results:
 - R-CHOP -14 superior to CHOP-14 in FFTF but not OS at 26 months
 - No significant difference between 6 and 8 cycles

Diffuse Large B-Cell NHL

Management of Elderly Patient

- Dutch HOVON and Nordic Lymphoma Groups
- High-risk elderly NHL patients
- Purpose: compare 8 cycles intensified CHOP (CHOP-14) vs R-CHOP 14
- Results:
 - Adding rituximab to CHOP-14 significantly improved OS
 - Control arm halted after interim analysis of 250
- Toxicity:
 - 30% unable to complete 6 cycles of R-CHOP
 - 20% unable to complete 6 cycles CHOP

Sonneveld, P., et al, Abstract#16, Blood 2005

Stem Cell Transplant For Older Patients

- Biologic behavior and responsiveness to treatment of many cancers not different based on age
- Other factors probably more important than chronologic age
 - Comorbid disease
 - Frailty
 - Functional status
 - Altered immune function

Stem Cell Transplant for Elderly NHL – Autologous HCT

Auto SCT well tolerated in patients over 60 with relapsed or refractory NHL Stamatouloullas et al BMT (1997) 19, 31-35

- Low toxicity and good QOL in elderly patients following auto HCT for hematologic malignancies
 - 48 patients median age 63 (20 pts with NHL)
 - QOL evaluated with QLQ-C30 questionnaire Olivieri et al. BMT (2001) 27, 1189-1195
- Autologous SCT in elderly patients with NHL
 - 26 patients, median age 66 years (range 60-78), Bu/Cy conditioning
 - All patients engrafted
 - The 100-day transplant mortality was 0% Yusef et al Abstract #5290 Blood 2005

Stem Cell Transplant for Elderly NHL – Allogeneic HCT

- Allogeneic SCT in patients with hematologic malignancies >60 years
 - Potentially curative
 - Reduced-intensity regimens available
 - Feasibility of reduced-intensity HCT regimens documented in elderly patients with AML and MDS (Abstract # 2892, Blood 2005)
- No increase in CMV reconstitution in older transplant patients who undergo reduced-intensity or non-myeloablative HCT Gallez-Hawkins, Abstract #2346, Blood 2005

Special Considerations For the Management of the Elderly Patient

- Elderly patients are less likely to get effective cancer treatment despite evidence that they can tolerate it
- Elderly patients are more likely to be improperly staged
- Under use of aggressive treatment is often assumed to be related to coexisting conditions
- Use of Comprehensive Geriatric Assessments is important

Comprehensive Geriatric Assessment

- Function
 - ADLs, performance status
- Comorbidity
 - Number of comorbid conditions and seriousness
- Socioeconomic status
 - Living conditions, presence/adequacy of caregiver, income, transportation
- Geriatric Syndromes
 - Dementia, depression, delirium, falls, osteoporosis, neglect/abuse, failure to thrive
- Polypharmacy
 - Number of meds, drug-drug interactions
- Nutrition
 - Nutritional risk

Supportive Care

- National Cancer Center Network Coalition recommends routine prophylactic use of growth factors in patients > 70 years treated with anthracycline-containing regimens
- American Society of Clinical Oncology guidelines report growth factor use may permit completion of chemotherapy in elderly patients with NHL

Supportive Care - Case Study

- 65 yo male with significant comorbidities dx with DLBC NHL in 1994
- Tx with CHOP x 6 followed by consolidative XRT
- Recurred 2003 tx with CHOP-R x 3 with no supportive care an tx stopped due to performance status
- Future ?

First-Cycle Pegfilgrastim Reduces Chemo-Induced Febrile Neutropenia among Older Patients with NHL

- Patients treated in community practice
- Increased age an established risk factor for chemo-induced neutropenia
- N=852
- Pegfilgrastim in first and subsequent cycles vs none following cycle 1 with subsequent use at MD discretion
- Results:
 - Overall incidence of febrile neutropenia lower in pegfilgrastim arm (15% vs 37%)
 - First cycle febrile neutropenia lower in pegfilgrastim arm (7% vs 25%)
 - Incidence of hospitalization lower (17% vs 37%)

Anemia in the Elderly and the Risk of Injurious Falls

- 30% community-dwelling elderly fall annually and risk increases to 50% by 80 years – 10% experience serious injuries
- **Purpose**: To investigate whether anemia increases risk of injurious falls (IF)
- **Methods**: Health claims data, 47,530 participants, anemia status based on WHO criteria
- **Results**: Linear trend of increasing falls with decreasing hemoglobin levels ($p < .001$).
- Incidence of IF was 15.8, 14.0, 9.8, and 6.5 per 1,000 person-years for Hb levels of <10 , $10-<12$, $12-<13$, and >13

Impact of Anemia on Medical Cost of Injurious Falls in the Elderly

- Falls in the elderly are a significant cause of functional disability and significantly increase health care burden
- **Purpose**: to determine if presence of anemia significantly increases medical costs related to falls
- **Methods**: 620 participants, Mean age 76.3 years, retrospective economic analysis of medical claims
- **Results**: difference in medical costs between patients with and without anemia increased significantly in the post-fall period. Average increase of \$1,855 - \$2,811 per patient per month ($p < .030$)

Lefebvre, P. et al., abstract#2238, *Blood*, Vol 106, Nov, 2005.

Images not available