Double-Hit Lymphoma: Practicing in a Data-Limited Setting

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Disclosures

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MedImmune - research funding (in)
Presentation Outline

- Definitions: double-hit lymphoma (DHL), double-expressor lymphoma (DEL)
- Clinical features of DHL and DEL
- Prognostic implications
- DHL management points
- DEL management points
- Relapsed or refractory DEL and DHL
- Are all DEL, DHL created equal?
- Conclusions
Diffuse Large B-cell Lymphoma
Outcomes in the 21st Century

Upfront Treatment of DLBCL:

![Graph A](image1)

Thomas M. Habermann et al. JCO 2006;24:3121-3127

Relapsed DLBCL:

![Graph B](image2)

Gisselbrecht et al. JCO 2010
DLBCL - Who Relapses?


Scott et al. *J Clin Oncol* 33:2848-2856
Are there better biomarkers in DLBCL?

- Aggressive B-cell NHLs exhibit:
  - Recurrent chromosomal rearrangements
    - MYC: 3-16% DLBCL, 33-80% BCLU, ~100% Burkitt
    - BCL6: 20-40% DLBCL
    - BCL2: 15-30% DLBCL
  - Over-expression of various proteins
    - MYC: 20-40% DLBCL/BCLU
    - BCL2: 60-80% DLBCL/BCLU
    - BCL6: 70-85% DLBCL/BCLU
MYC, BCL2, and BCL6


MYC, BCL2, and BCL6

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• Conclusions
Definitions: Double-Hit Lymphoma (DHL)

- Aggressive B-cell lymphoma (DLBCL) with rearrangement of MYC and BCL2 and/or BCL6
  - 2-10% of newly diagnosed DLBCL

FISH with dual color break-apart probes for MYC, BCL2, BCL6. Photos courtesy of V. Bedell, 63x Bioview imaging system.
Definitions: Double-Hit Lymphoma (DHL)

• % of $MYC$-rearranged nuclei – varying thresholds (5%, 10%, 20% of nuclei rearranged)

• $MYC+BCL2$ rearranged vs $MYC+BCL6$ rearranged – different outcomes?
MYC/BCL2-DH vs MYC/BCL6-DH

Ye et al. Oncotarget 2016
Definitions: Double-Hit Lymphoma (DHL)

- % of MYC-rearranged nuclei – varying thresholds (5%, 10%, 20% of nuclei rearranged)

- **MYC**+**BCL2** rearranged vs **MYC**+**BCL6** rearranged – different outcomes?

- “Atypical” DHL – what about copy gain of **MYC**, **BCL2**, **BCL6**?
“Atypical” DHL – Copy Gain

- Conflicting data – alternate chromosome alterations not clearly associated with outcome


Li et al. Mod Pathol. 2015 Feb;28(2):208-17.
Definitions: Double Expressor Lymphoma (DEL)

- DLBCL with coexpression of MYC and BCL2 proteins by immunohistochemistry – 21-34% of newly diagnosed DLBCL

Photos courtesy of S. Rodig, 1000x
Definitions: Double Expressor Lymphoma (DEL)

• Subjectivity is an issue - MYC/BCL2 scored visually by pathology
• Different thresholds used in different studies to define MYC/BCL2 positive
  – Most common: MYC ≥ 40%, BCL2 ≥ 50%
  – Others: MYC/BCL2 ≥ 40/70, 40/30, 50/30
• BCL6 expression is not relevant!
  – In fact, studies have shown BCL6 overexpression (> 25%) was more favorable
MYC+ Aggressive B-NHL is a Continuum
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• Clinical features of DHL and DEL

• Prognostic implications

• DHL management points

• DEL management points

• Relapsed or refractory DEL and DHL

• Conclusions
Clinical features: Cell-of-Origin, DHL, and DEL

- DHL usually GCB subtype: 64-95%
- DEL usually non-GCB subtype: 58-76%

Hu et al Blood 2013 121: 4021-4031
**DEL and DHL – High-risk clinical features**

- DHL tend to be high stage, high LDH, extranodal, +BM

### Table 1. Baseline characteristics of patients with cytogenetic double hit lymphomas in selected studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>n DHL/total (%)</th>
<th>Male (%)</th>
<th>Median age, years</th>
<th>Prior indolent lymphoma</th>
<th>Stage III/IV (%)</th>
<th>LDM &gt;ULN (%)</th>
<th>B symptoms (%)</th>
<th>&gt;1 LN site (%)</th>
<th>CNS+ (%)</th>
<th>BM+ (%)</th>
<th>IPI ≥4 (%)</th>
<th>GCB type (%)</th>
<th>Median IPI 67, %</th>
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<tbody>
<tr>
<td>Johnson et al (2009)</td>
<td>54/54</td>
<td>32 (59)</td>
<td>NR</td>
<td>20 (37)</td>
<td>41 (76)</td>
<td>27 (50)</td>
<td>NR (19 (35))</td>
<td>NR (32 (59))</td>
<td>NR (14 (26))</td>
<td>NR (34 (63))</td>
<td>NR (10 (30))</td>
<td>NR (24 (77))</td>
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<td>Niitsu et al (2009)</td>
<td>19/394 (4.8)</td>
<td>10 (53)</td>
<td>61</td>
<td>NR</td>
<td>19 (100)*</td>
<td>19 (100)*</td>
<td>NR</td>
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<td>NR</td>
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<td>Tomita et al (2009)</td>
<td>27/27* (100)</td>
<td>15/27 (56)</td>
<td>51</td>
<td>5/23 (22)</td>
<td>22/23 (96)</td>
<td>25/27 (92)</td>
<td>NR</td>
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<td>NR</td>
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<tr>
<td>Barrans et al (2010)</td>
<td>27/303* (8.6)</td>
<td>15 (43)</td>
<td>65.5</td>
<td>NR</td>
<td>21 (69)*</td>
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<tr>
<td>Snuderl et al (2010)</td>
<td>20/60 (33)</td>
<td>11 (55)</td>
<td>63*</td>
<td>6 (30)</td>
<td>18 (90)</td>
<td>Med 3.5</td>
<td>NR</td>
<td>NR</td>
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<td>NR</td>
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<td>NR (80)</td>
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<td>Pedersen et al (2012, 2014)</td>
<td>23/228 (10)</td>
<td>11 (48)</td>
<td>64</td>
<td>10 (42)</td>
<td>19 (83)</td>
<td>14/17 (82)</td>
<td>NR</td>
<td>8/17 (47)</td>
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<td>NR</td>
<td>NR</td>
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<td>Oki et al (2014)</td>
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<td>84 (65)</td>
<td>62</td>
<td>14 (11)</td>
<td>109 (84)</td>
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<td>Petrich et al (2014)</td>
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<td>67 (22)</td>
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Cheah et al. BJH 2015
## DEL and DHL – High-risk clinical features

### Table 1. Clinicopathological characteristics and outcome of DLBCLs treated with R-CHOP

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall</th>
<th>OS, P</th>
<th>PFS, P</th>
<th>DP</th>
<th>Non-DP</th>
<th>P value</th>
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<tbody>
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<td><strong>Patients</strong></td>
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<td>157 (100)</td>
<td>309 (100)</td>
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<td>Male</td>
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<td>.4730</td>
<td>90 (57)</td>
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<td>67 (43)</td>
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<td>≤60</td>
<td>194 (42)</td>
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<td>106 (69)</td>
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<td><strong>B symptoms</strong></td>
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<td>Absence</td>
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<td><strong>ECOG performance status</strong></td>
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<td>≤2</td>
<td>360 (88)</td>
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<td>111 (83)</td>
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<td>I-II</td>
<td>219 (49)</td>
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<td>&lt;.0001</td>
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<td>0-2</td>
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<td>3-5</td>
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<td><strong>Tumor size, cm</strong></td>
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<td>≤7.5</td>
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<td>&gt;7.5</td>
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<td><strong>Treatment response</strong></td>
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<tr>
<td>CR</td>
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<td>&lt;.0001</td>
<td>103 (58)</td>
<td>251 (84)</td>
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<td>Others</td>
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<td>48 (16)</td>
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<td><strong>COO classification</strong></td>
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<td>GCB</td>
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<td><strong>Ki-67</strong></td>
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<td>≤70</td>
<td>188 (34)</td>
<td>.2938</td>
<td>.3434</td>
<td>41 (26)</td>
<td>117 (36)</td>
<td>.0386</td>
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<td>&gt;70</td>
<td>304 (56)</td>
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<td>116 (74)</td>
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<td><strong>TP53 mutations</strong></td>
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<td>Absence</td>
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<tr>
<td>Presence</td>
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<td></td>
<td>40 (25)</td>
<td>69 (22)</td>
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</table>

Hu et al. Blood 2013
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• Definitions: double-hit lymphoma (DHL), double-expressor lymphoma (DEL)
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DHL: Outcomes with R-CHOP

Johnson et al. Blood 2009
DHL: Outcomes with R-CHOP

Hu et al.  
Blood 2013
DEL: Outcomes with R-CHOP

Green et al. JCO 2012
DEL: Outcomes with R-CHOP

Hu et al.
Blood 2013
Outcomes in DEL and DHL after R-CHOP

Johnson et al. JCO 2012

Overall Survival (proportion)

Time (years)

Other (n = 236)
MYC⁺/BCL2⁺ (n = 55)
DHIT (n = 14)
Neither

P < .001
*P = .014 (MYC⁺/BCL2⁺ vs other)
DEL is prognostic even in non-DHL

D

No MYC/BCL2 DH

All others (n=260)

p<.0001

MYC+BCL2+ (n=124)

Hu et al.
Blood 2013
DEL is prognostic independent of COO

Green et al. JCO 2012
DEL is prognostic independent of IPI

Green et al. JCO 2012
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DHL Management Points

1. Intensive upfront regimens
2. CNS prophylaxis
3. Consolidative stem cell transplantation
Intensive Regimens vs R-CHOP for DHL

Petrich AM et al Blood 2014
Intensive Induction Regimens for DHL

Oki Y et al BJH 2014
### Intensive regimens: Magrath?

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number</th>
<th>Age &lt; 60</th>
<th>DH/TH at Transformation of low grade</th>
<th>DLBCL Morphology</th>
<th>ASCT in CR1</th>
<th>Achieved EFS12</th>
<th>Median OS (months)</th>
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</thead>
<tbody>
<tr>
<td>R-CHOP</td>
<td>33</td>
<td>36%</td>
<td>9%</td>
<td>59%</td>
<td>12%</td>
<td>31%</td>
<td>17.7</td>
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<tr>
<td>R-EPOCH</td>
<td>17</td>
<td>35%</td>
<td>29%</td>
<td>36%</td>
<td>17%</td>
<td>47%</td>
<td>13.5</td>
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<tr>
<td>R-CODOX-M/IVAC</td>
<td>15</td>
<td>93%</td>
<td>7%</td>
<td>22%</td>
<td>33%</td>
<td>69%</td>
<td>Not reached</td>
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<tr>
<td>R-HyperCVAD</td>
<td>6</td>
<td>50%</td>
<td>33%</td>
<td>0%</td>
<td>0%</td>
<td>33%</td>
<td>12.3</td>
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</table>

Habermann et al. ASH 2016
CNS prophylaxis for DHL

Oki Y et al BJH 2014

Petrich AM et al Blood 2014
Why we consider consolidation…

(C) Overall Survival (probability)

- Salvage Therapy (N=84)
- Unknown or No Salvage Therapy (N=70)

log rank p=0.029

(P) Percent of patients

Number at risk

Time (Months)

Oki Y et al BJH 2014

Petrich AM et al Blood 2014
Consolidative Stem Cell Transplant in First Remission

Petrich AM et al Blood 2014
Consolidative Stem Cell Transplant in First Remission

Oki Y et al BJH 2014
Outcomes without consolidative SCT

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DEL Management Points

1. Intensive upfront regimens
2. CNS prophylaxis
3. Consolidative stem cell transplantation
Intensive treatment for DEL?

All patients (n = 71, 20 DEL)

ASCT patients (n = 55, 16 DEL)

Maura et al. EHA 2016
CNS Relapse Risk in DEL

Consolidative Autotransplant for DEL?

Puvvada SD et al. BJH 2016
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Relapsed/Refractory (R/R) Diffuse Large B-cell Lymphoma (DLBCL)

- ~25-40% of DLBCL patients
- SOC is salvage chemotherapy followed by autologous stem cell transplantation (ASCT) in chemosensitive patients
Relapsed or Refractory DEL/DHL

**Graph C**
- Overall Survival (probability) vs Time from Diagnosis (months)
- Lines represent different therapeutic approaches:
  - Salvage Therapy (N=84)
  - Unknown or No Salvage Therapy (N=70)
- Log rank p=0.029

**Graph F**
- Post-progression OS
- Percent of patients vs Time (Months)

Petrich AM et al Blood 2014

Oki Y et al BJH 2014
Rel/Ref DLBCL – CORAL study

396 patients with relapsed DLBCL

R-DHAP x 3

R-ICE x 3

BEAM - ASCT

Gisselbrecht et al. JCO 2010
161 had adequate tissue for FISH
28 (17%) were MYC-rearranged (MYC+), 75% were DHL
CR to salvage (either) worse in all MYC+, 25% vs. 45%
Fewer MYC+ went to autoSCTx (43% vs. 60%)

Progression free survival
4y PFS 18% (MYC+) vs 42%
Transplanted MYC+: 4y PFS 14%

Cuccuini et al. Blood 2012
Double Expressing (MYC/BCL2) and Double Hit Diffuse Large B-cell Lymphoma Have Inferior Survival After Autologous Stem Cell Transplantation


City of Hope (COH) and Dana-Farber Cancer Institute (DFCI)

American Society of Hematology Annual Meeting 2015
Cohort and Methods

- Retrospective study of 201 patients with R/R DLBCL who underwent ASCT at COH or DFCI/BWH from 2000-2013
  - All patients with archival tissue included

- IHC for MYC and BCL2 (Ventana, BOND)
  - 2-3 pathologists at each institution, scored in deciles

- FISH for MYC; BCL2, BCL6 in MYC-rearranged (dual-color break-apart, Abbott)
  - Abnormal value cutoff $\geq 10\%$ nuclei
### Immunohistochemistry Results

<table>
<thead>
<tr>
<th></th>
<th>Myc evaluable</th>
<th>Bcl2 evaluable</th>
</tr>
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<tbody>
<tr>
<td>Median (range)</td>
<td>186 (93%)</td>
<td>188 (94%)</td>
</tr>
<tr>
<td>30% (0-100%)</td>
<td>30% (0-100%)</td>
<td>90% (0-100%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Myc and Bcl2 performed</th>
<th>185</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥40%//  ≥50% (DEL)</td>
<td>74 (40%)</td>
</tr>
<tr>
<td>≥50%//  ≥50%</td>
<td>64 (35%)</td>
</tr>
<tr>
<td>≥40%//  ≥70%</td>
<td>67 (36%)</td>
</tr>
<tr>
<td>≥50%//  ≥70%</td>
<td>58 (31%)</td>
</tr>
</tbody>
</table>
DEL (MYC+/BCL2+ by IHC) Associated with Poorer Progression-Free Survival

Not DEL, n = 111

DEL, n = 74

4y PFS
DEL 37%, (95CI 26-48%)
Non-DEL 52%, (95CI 42-61%)

p = 0.001
DEL (MYC+/BCL2+ by IHC) Associated with Poorer Overall Survival

Not DEL, n = 111
DEL, n = 74

4y OS
DEL 52%, (95CI 39-63%)
Non-DEL 69%, (95CI 59-77%)  p = 0.005
## FISH Results

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Myc evaluable</strong></td>
<td>164 (82%)</td>
</tr>
<tr>
<td><strong>Not rearranged</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Myc-Rearranged</strong></td>
<td>137/164 (84%)</td>
</tr>
<tr>
<td><strong>Myc alone</strong></td>
<td>27/164 (16%)</td>
</tr>
<tr>
<td><strong>Double-hit (DHL)</strong></td>
<td>7 (4%)</td>
</tr>
<tr>
<td><strong>Myc/Bcl2</strong></td>
<td>20/164 (12%)</td>
</tr>
<tr>
<td><strong>Myc/Bcl6</strong></td>
<td>9 (5%)</td>
</tr>
<tr>
<td><strong>Myc/Bcl2/Bcl6</strong></td>
<td>6 (4%)</td>
</tr>
<tr>
<td><strong>Myc/Bcl2/Bcl6</strong></td>
<td>5 (3%)</td>
</tr>
</tbody>
</table>
DHL by FISH Associated with Poorer Progression-Free Survival

4y PFS
DHL 25%, (95CI 8-48%)
Non-DHL 48%, (95CI 39-56%)

Non-DHL, n = 144
DHL, n = 20
p = 0.007
DHL by FISH Associated with Poorer Overall Survival

4y OS
DHL 34\%, (95CI 13-57\%)
Non-DHL 63\%, (95CI 53-71\%)
p = 0.003
# ASCT Outcomes in R/R DEL and DHL

![Progression-Free Survival Graph](image)

<table>
<thead>
<tr>
<th>Variable</th>
<th>OS</th>
<th>P</th>
<th>PFS</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td></td>
<td>HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Neither DEL nor DHL</td>
<td>Ref</td>
<td></td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>DEL</td>
<td>1.8 (0.9 to 3.2)</td>
<td>.075</td>
<td>1.8 (1.05 to 3.2)</td>
<td>.035</td>
</tr>
<tr>
<td>DHL</td>
<td>3.4 (1.5 to 7.6)</td>
<td>.004</td>
<td>2.9 (1.3 to 6.3)</td>
<td>.009</td>
</tr>
<tr>
<td>Disease status at ASCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>Ref</td>
<td></td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>2.4 (1.3 to 4.4)</td>
<td>.007</td>
<td>1.7 (1.0 to 2.9)</td>
<td>.075</td>
</tr>
</tbody>
</table>

Herrera et al. *JCO* 2016
Double-Hit and Double-Expressor Lymphomas Are Not Associated With An Adverse Outcome After Allogeneic Stem Cell Transplantation


City of Hope (COH) and Dana-Farber Cancer Institute (DFCI)

American Society of Hematology Annual Meeting 2016
Rationale

• Poorer ASCT outcome in R/R DEL and DHL patients (Herrera et al. *JCO* 2016)
  – 50% of R/R DLBCL pts never make it to ASCT (Gisselbrecht et al. *JCO* 2010)

• Allogeneic SCT (alloSCT) produces durable remission in a proportion of R/R DLBCL pts who fail or are not candidates for ASCT (Fenske et al. *BJH* 2016, Bacher et al. *Blood* 2012)

• Can alloSCT overcome the chemoresistance of DEL/DHL in pts with R/R DLBCL?
Cohort and Methods

- Retrospective study of patients with R/R DLBCL or transformed indolent lymphoma (TIL) who underwent alloSCT at COH, MGH, or DFCI/BWH from 1/2000-5/2014
  - All patients with archival tissue included

- IHC for MYC and BCL2 (Ventana, BOND)
  - 2-3 pathologists at each institution, scored in deciles

- FISH for MYC; BCL2, BCL6 in MYC-rearranged (dual-color break-apart, Abbott)
  - MYC rearrangement cutoff ≥ 10% nuclei
# IHC and FISH Results

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>78 (100%)</td>
<td></td>
</tr>
<tr>
<td><strong>IHC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MYC expression median (range)</td>
<td>40% (0-90%)</td>
<td></td>
</tr>
<tr>
<td>BCL2 expression median (range)</td>
<td>90% (0-100%)</td>
<td></td>
</tr>
<tr>
<td><strong>DEL (MYC≥40%/BCL2≥50%)</strong></td>
<td>37 (47%)</td>
<td></td>
</tr>
<tr>
<td><strong>FISH</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DHL (any)</strong></td>
<td>10 (13%)</td>
<td></td>
</tr>
<tr>
<td>MYC/BCL2/no BCL6</td>
<td>5 (6%)</td>
<td></td>
</tr>
<tr>
<td>MYC/BCL6/no BCL2</td>
<td>3 (4%)</td>
<td></td>
</tr>
<tr>
<td>MYC/BCL2/BCL6</td>
<td>2 (3%)</td>
<td></td>
</tr>
</tbody>
</table>

- No significant difference in any clinical characteristic in patients with DEL vs DHL vs neither abnormality.
DEL: No Significant Association with Progression-Free Survival

4y PFS
DEL 30%, (95CI 16-46%)
Non-DEL 39%, (95CI 24-54%)

p = 0.2
DEL: No Significant Association with Overall Survival

4y OS
DEL 31%, (95CI 16-47%)
Non-DEL 49%, (95CI 32-63%)  p = 0.17

Not DEL, n = 41
DEL, n = 37
DHL: No Association with Progression-Free Survival

DHL, n = 10
Non-DHL, n = 68

4y PFS
DHL 40%, (95CI 12-67%)
Non-DHL 34%, (95CI 22-46%)

p = 0.6
DHL: No Association with Overall Survival

DHL, n = 10
Non-DHL, n = 68

4y OS
DHL  50%, (95CI 18-75%)
Non-DHL 38%, (95CI 26-50%)  p = 0.5
DHL vs DEL (non-DHL) vs Neither

DHL, n = 10
DEL (non-DHL), n = 31
Neither, n = 37

4y PFS
DHL 40%, (95CI 12-67%) p = 0.6
DEL (non-DHL) 29%, (95CI 14-47%)
Neither 38%, (95CI 22-54%)
## Multivariable Analysis: PFS

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR for PFS</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;=55</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>&gt;55</td>
<td>0.4</td>
<td>0.011</td>
</tr>
<tr>
<td><strong>Disease status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR/unk</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>SD/PD</td>
<td>2.4</td>
<td>0.020</td>
</tr>
<tr>
<td><strong>Disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLBCL/BCL-U</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>TIL</td>
<td>0.5</td>
<td>0.035</td>
</tr>
<tr>
<td>DEL</td>
<td>1.2</td>
<td>0.5</td>
</tr>
<tr>
<td>DHL</td>
<td>0.9</td>
<td>0.8</td>
</tr>
</tbody>
</table>
Presentation Outline

• Definitions: double-hit lymphoma (DHL), double-expressor lymphoma (DEL)
• Clinical features of DHL and DEL
• Prognostic implications
• DHL management points
• DEL management points
• Relapsed or refractory DEL and DHL
• Are all DEL, DHL created equal?
• Conclusions
Are all DHL created equal? Translocation partner may matter

- *Ig* vs non-*Ig* translocation partner

Copie-Bergman et al. Blood 2015
Are all DHL created equal? Translocation partner may matter

Pedersen et al. Eur J Hematology 2014

Johnson et al. Blood 2009
DEL+DHL vs isolated DEL or DHL

Johnson et al. Blood 2009
DEL+DHL vs isolated DEL or DHL

Herrera et al. JCO 2016
Take Home Messages

• DHL = 2-10% of newly dx DLBCL
• DEL = 25-35% of newly dx DLBCL

• DEL and DHL: high-risk clinical features

• DEL and DHL: poor outcomes with R-CHOP
Take Home Messages

- DHL: Intensive regimens, CNS ppx, consider autotransplant in CR1
- DEL: consider intensive tx and CNS ppx
- Relapsed or refractory DEL or DHL: inferior outcomes should be enrolled on clinical trials
- Not all DEL or DHL are created equal?
Thank you!