Aggressive Lymphomas

Mantle cell lymphoma
Large cell lymphoma
T cell lymphoma

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Lymphoma Program
Hematology/Oncology
Please note that some of the studies reported in this presentation were presented as an abstract and/or presented at a conference. These data and conclusions should be considered to be preliminary until published in a peer-reviewed journal.
Mantle Cell Lymphoma

- Uncommon subtype of NHL, with features of both indolent and aggressive disease
- 74% male, median age 63 years
- >80% stage III/IV including marrow involvement
- Extranodal sites common: lymphomatous polyposis, gastrointestinal, soft tissue, or peripheral blood
- Sensitive to chemotherapy, but prone to relapse
Rituximab + HyperCVAD/M-A in Previously Untreated MCL: Efficacy at 10 Year Follow-up

- N = 97; median follow up of 8 years
- CR/CRu: 87%
- OS: 68% @ 8 yrs for age ≤ 65 yrs; 33% for > 65 yrs
- TTF: 46% @ 8 yrs for age ≤ 65 yrs; 16% for > 65 yrs

Romaguera BJH 2010;151(1):111
There were 6 (3.8%) treatment-related deaths

- MCL2 survival (n = 160): 73%
- MCL2 RD (n = 145) 5-year DOR: 72%
- MCL2 EFS (n = 160): 63%

EFS, MCL1 versus MCL2: p < .0001

Geisler *Blood* 2008;112(7):2687
UPenn MCL experience 2005-2010

PFS

Percent survival vs Years

- R-HCVAD +ASCT
- R-CHOP +ASCT
- R-HCVAD
- R-CHOP
Benefit of Maintenance

![Graph showing survival rates over years for different treatment regimens: RHCVAD alone, RHCVAD + Rituxan maintenance, and RHCVAD + auto SCT. The graph plots percent survival on the y-axis and years on the x-axis, illustrating the benefit of maintenance therapy.]
Bortezomib Maintenance Therapy after Induction with R-CHOP, ARA-C and Autologous Stem Cell Transplantation in Newly Diagnosed MCL Patients, Results of a Multicenter Phase II HOVON Study

by Jeanette K Doorduijn, Monique C. Minnema, Marie Jose Kersten, Pieternella J Lugtenburg, Martin R. Schipperus, Marinus van Marwijk Kooy, Marius MacKenzie, Josée M Zijlstra, Henriette W Berenschot, M. R Schaafsma, Dana A Chitu, and Hanneke C. Kluin-Nelemans

Blood
Volume 126(23):339-339
December 3, 2015

EFS from randomization (mnth)
Rnr 2 rand. arm

Cumulative percentage

No further treat 30 9
Bortezomib maint 30 8
Cox LR P = 0.73

No further treat

At risk: 30 25 23 15 8 5 2 0
Bortezomib maint 30 29 25 17 11 6 2 0

Bortezomib maint
Bortezomib Maintenance (BM) Versus Consolidation (BC) Following Aggressive Immunochemotherapy and Autologous Stem Cell Transplant (ASCT) for Untreated Mantle Cell Lymphoma (MCL): CALGB (Alliance) 50403


Blood
Volume 126(23):337-337
December 3, 2015
Product-Limit Survival Estimates

Survival Probability

Years from study entry

+ Censored
Logrank p=0.0030

MRD negative positive

No. of Subjects Event Censored Median Survival (95% CL)
negative 15 1 14 . ( . . )
positive 32 17 15 5.3 ( 3.3 . )

Lawrence D. Kaplan et al. Blood 2015;126:337
Predictive Power of Early, Sequential MRD Monitoring in Peripheral Blood and Bone Marrow in Patients with Mantle Cell Lymphoma Following Autologous Stem Cell Transplantation with or without Rituximab Maintenance; Interim Results from the LyMa-MRD Project, Conducted on Behalf of the Lysa Group

- The estimated 3y-PFS: according to BM and PB MRD status
  - MRD pos/obs 61.6% (IC95%, 35.4-79.8) / 51.8% (IC95%, 24.4-73.6)
  - MRD neg/obs 83.9% (IC95%, 70.1-91.7)/ 86.5% (IC95%, 73.5-93.4)
  - pos/RM 86.2% (IC95%, 67.3-94.6)/ 80% (IC95%, 50-93.1)
  - neg/RM patients 91.8% (IC95%, 76.3-97.3), (p=0.0110)/92.8% (IC95%, 81.6-97.3) (p=0.0027),
Bendamustine

- R Bendamustine vs CHOP-R
  - Rummel et al, STiL NHL-1
  - Indolent lymphoma subtypes
  - Better toxicity profile
  - Improved PFS
Combination of lenalidomide and rituximab overcomes rituximab-resistance in patients with indolent B-cell and mantle cell Lymphomas

Elise A. Chong,1 Tahamtan Ahmadi,1 Nicole A. Aqui,1 Jakub Svoboda,1 Sunita D. Nasta,1 Anthony R. Mato,1 Kristy M. Walsh,1 and Stephen J. Schuster1

Phase II trial: lenalidomide-rituximab in patients with indolent B-cell or mantle cell lymphomas who were previously defined as rituximab-resistant. 43 pts: ORR after 8 weeks of lenalidomide was 30.2%; the ORR increased to 62.8% after the addition of rituximab to lenalidomide. Median follow-up 39.2 months, median PFS is 22.2 months and median response duration is 24 months.
Lenalidomide and Rituximab for Untreated Indolent Lymphoma: Final results of a Phase II Study

### Efficacy

<table>
<thead>
<tr>
<th>Efficacy, %</th>
<th>All (N=103)</th>
<th>FL (N=46)</th>
<th>SLL (N=30)</th>
<th>MZL (N=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>90</td>
<td>98</td>
<td>80</td>
<td>89</td>
</tr>
<tr>
<td>CR/CRu</td>
<td>64</td>
<td>87</td>
<td>27</td>
<td>67</td>
</tr>
<tr>
<td>PR</td>
<td>26</td>
<td>11</td>
<td>53</td>
<td>22</td>
</tr>
<tr>
<td>SD</td>
<td>8</td>
<td>2</td>
<td>13</td>
<td>11</td>
</tr>
</tbody>
</table>

- 2-year PFS = 83% for all pts; 89% for FL
- Molecular response in most FL patients with the absence of detectable BCL-2
- 93% of 45 FL PET+ pts attained complete metabolic response
- Two episodes of neutropenic fever
Jia Ruan, MD, PhD et al November 15, 2013; Blood: 122 (21)

- Lenalidomide 20 mg daily on days 1-21 of a 28-day cycle x12 cycles, with dose escalation to 25 mg daily if tolerated.
- Standard dose rituximab is administered weekly x 4 during cycle 1, then once every other cycle, for a total of 9 doses.
- Maintenance phase after cycle 13, lenalidomide is administered at 15 mg daily on days 1-21 of a 28-day cycle, with rituximab maintenance once every other cycle until progression of disease.
- ORR for evaluable patients is 77% (95% CI = 57% to 89%) with 40% CR/CRu (95% CI = 23% to 59%).
- Median progression-free survival and duration of response have not been reached
BTKi

- Bruton Tyrosine Kinase inhibitors: ibrutinib (PCI-32765)
  - Objective responses in 7 of 9 patients
  - 68 patients in Phase II 69% ORR
    - Stratified by prior velcade
Follow up studies

- Wang, Abst 627 ASH 2014
- Phase 2 trial in relapsed disease
- Ibrutinib and rituximab induction. After 2 years, ibrutinib alone
- ORR 68%, 40% CR
- Better for pts with lower proliferative rate (Ki67 < 50% with ORR 100%; > 50% ORR 50%)
Ibrutinib Vs Temsirolimus: Results from a Phase 3, International, Randomized, Open-Label, Multicenter Study in Patients with Previously Treated Mantle Cell Lymphoma (MCL)


Blood
Volume 126(23):469-469
December 3, 2015
Figure 1. IRC-Assessed PFSa

*Intent-to-treat population
Median follow-up: 20.0 months

<table>
<thead>
<tr>
<th></th>
<th>Ibrutinib</th>
<th>Temsirolimus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS (months)</td>
<td>14.6</td>
<td>6.2</td>
</tr>
<tr>
<td>HR</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>0.32-0.58</td>
<td></td>
</tr>
<tr>
<td>Log-rank p value</td>
<td>&lt;0.0001</td>
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</tr>
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Alive without progression (%)

Subjects at risk

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<thead>
<tr>
<th>Group</th>
<th>139</th>
<th>114</th>
<th>101</th>
<th>83</th>
<th>77</th>
<th>45</th>
<th>34</th>
<th>8</th>
<th>5</th>
<th>0</th>
<th>0</th>
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</thead>
<tbody>
<tr>
<td>Ibrutinib</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temsirolimus</td>
<td>141</td>
<td>93</td>
<td>69</td>
<td>45</td>
<td>33</td>
<td>19</td>
<td>11</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>

Simon Rule et al. Blood 2015;126:469
Table 1. Safety Overview

<table>
<thead>
<tr>
<th>Category</th>
<th>Term</th>
<th>Any Grade/Grade $\geq 3$, %</th>
<th>Ibrutinib</th>
<th>Temsirolimus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td></td>
<td></td>
<td>18.0</td>
<td>9.4</td>
</tr>
<tr>
<td>Anemia</td>
<td></td>
<td></td>
<td>18.0</td>
<td>7.9</td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td></td>
<td>28.8</td>
<td>2.9</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
<td>22.3</td>
<td>4.3</td>
</tr>
<tr>
<td>Neutropenia</td>
<td></td>
<td></td>
<td>15.8</td>
<td>12.9</td>
</tr>
<tr>
<td>Epistaxis</td>
<td></td>
<td></td>
<td>8.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Cough</td>
<td></td>
<td></td>
<td>22.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td></td>
<td></td>
<td>12.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td></td>
<td>14.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Pyrexia</td>
<td></td>
<td></td>
<td>16.5</td>
<td>0.7</td>
</tr>
<tr>
<td>Stomatitis</td>
<td></td>
<td></td>
<td>2.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Grade $\geq 3$ atrial fibrillation</td>
<td></td>
<td></td>
<td>3.6</td>
<td>1.4</td>
</tr>
<tr>
<td>Grade $\geq 3$ bleeding</td>
<td></td>
<td></td>
<td>7.9</td>
<td>5.0</td>
</tr>
<tr>
<td>Major hemorrhage</td>
<td></td>
<td></td>
<td>10.1</td>
<td>6.5</td>
</tr>
<tr>
<td>Secondary malignancy</td>
<td></td>
<td></td>
<td>3.6</td>
<td>2.9</td>
</tr>
</tbody>
</table>

$^a$Rates shown are not adjusted for differences in exposure (median treatment duration was 14.4 months for ibrutinib and 3.0 months for temsirolimus).

$^b$Major hemorrhage includes grade $\geq 3$ hemorrhage, central nervous system hemorrhage, and serious bleeding events of any grade.

Simon Rule et al. Blood 2015;126:469
Idelalisib in MCL

CAL101: Best Tumor Response in CLL, Indolent NHL, and MCL (N = 63)

Anti-tumor response (> 50% reduction) was observed at every dose level evaluated, with no obvious dose response.

Kaplan–Meier Curves for Progression-free Survival and Overall Survival.

A Progression-free survival
- All patients
- No 17p or 11q deletions (n=29)
- 11q deletion (n=23)
- 17p deletion (n=28)

P=0.04 by log-rank test

B Overall Survival
- All patients
- No 17p or 11q deletions (n=29)
- 11q deletion (n=23)
- 17p deletion (n=28)

P=0.15 by log-rank test

- Mutated IGHV (n=12)
- Unmutated IGHV (n=69)

P=0.67 by log-rank test

- Mutated IGHV (n=12)
- Unmutated IGHV (n=69)

P=0.86 by log-rank test

Kaplan–Meier Curves for Secondary End Points.

A. Time to Response
   - Median, 1.9 mo (N=71)
   - No. at Risk: 40, 59, 66, 68

B. Duration of Response
   - Median, 12.5 mo (N=71)
   - No. at Risk: 71, 54, 34, 17, 9, 0, 0

C. Progression-free Survival
   - Median, 11 mo (N=125)
   - No. at Risk: 125, 100, 59, 39, 20, 13, 0

D. Overall Survival
   - Median, 20.3 mo (N=125)
   - No. at Risk: 125, 118, 105, 68, 38, 23, 12, 4, 0
MCL: Summary

- **Induction**
  - High response rates can be achieved with rituximab + chemotherapy, but patients are unlikely to be cured with chemotherapy alone

- **Consolidation**
  - HDT with ASCT appears to improve the TTF; survival benefit remains to be proven

- **Newer targeted agents and cellular therapies are changing the landscape of therapy**
Diffuse Large Cell Lymphoma

- Most frequent subtype of non-Hodgkin’s lymphoma
  - 30-35% of all cases
- Prototype of aggressive lymphoma
  - Complete remissions with effective therapy
  - Significant percentage of patients may be cured
    - Dependent on both patient and tumor characteristics
Key oncogenic pathways in DLBCL. The 2 major molecular subtypes of DLBCL are shown: the GCB and the ABC type.

Sehn L H, and Gascoyne R D Blood 2015;125:22-32
## Select novel targeted agents under evaluation in DLBCL

<table>
<thead>
<tr>
<th>Agent</th>
<th>Target</th>
<th>Molecular subgroup</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bortezomib</td>
<td>NF-κB</td>
<td>ABC</td>
</tr>
<tr>
<td>Fostamatinib</td>
<td>SYK</td>
<td>ABC</td>
</tr>
<tr>
<td>Ibrutinib</td>
<td>BTK</td>
<td>ABC</td>
</tr>
<tr>
<td>Enzastaurin</td>
<td>PKCβ</td>
<td>ABC</td>
</tr>
<tr>
<td>Idelalisib</td>
<td>PI3K</td>
<td>(?) GCB</td>
</tr>
<tr>
<td>ABT-199</td>
<td>BCL2</td>
<td>(?) GCB, dual expressers</td>
</tr>
<tr>
<td>EZH2 inhibitors</td>
<td>EZH2</td>
<td>GCB</td>
</tr>
<tr>
<td>BCL6 inhibitors</td>
<td>BCL6</td>
<td>GCB</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>Microenvironment, NF-κB</td>
<td>ABC</td>
</tr>
<tr>
<td>Obinutuzumab</td>
<td>CD20</td>
<td>All</td>
</tr>
<tr>
<td>Ofatumomab</td>
<td>CD20</td>
<td>All</td>
</tr>
<tr>
<td>Polatuzumab vedotin</td>
<td>CD79b</td>
<td>All</td>
</tr>
</tbody>
</table>
DLCL: Beyond RCHOP


- **Brentuximab Vedotin with RCHOP As Frontline Therapy in Patients with High-Intermediate/High-Risk Diffuse Large B Cell Lymphoma (DLBCL): Results from an Ongoing Phase 2 Study** Blood 2015 126:814; Christopher A. Yasenchak et al

- **A Prospective Randomised Trial of Targeted Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) Based upon Real-Time Gene Expression Profiling: The Remodl-B Study of the UK NCRI and SAKK Lymphoma Groups (ISRCTN51837425)** Blood 2015 126:812; Andrew J Davies et al


Optimization of Rituximab for Treatment of DLBCL in Young, High-Risk Patients-Results of the Dense-R-CHOEP Trial of the German High-Grade Lymphoma Study Group_Blood 2015 126:474; Norbert Schmitz, Maike Nickelsen, Marita Ziepert, Mathias Haenel, Andreas Viardot, Martin H. Dreyling, Peter Borchmann, Carsten Bokemeyer, Christian Peschel, Hans-
Phase 1 Trial Testing Single Agent CUDC-907, a Novel, Oral Dual Inhibitor of Histone Deacetylase (HDAC) and PI3K: Initial Assessment of Patients with Relapsed or Refractory (RR) Diffuse Large B-Cell Lymphoma (DLBCL), Including Double Expressor (DE) Lymphoma

- **Blood: 126 (23)** Anas Younes, MD

- 63 pts with lymphoma or multiple myeloma

- CUDC-907 in 21-day cycles according to once daily (QD), intermittent (BIW or TIW), or five days on/two days off (5/2) dosing schedules.

- A dose expansion using the 60 mg 5/2 dose and schedule is ongoing.

- Among 11/18 subjects with RR DLBCL who were evaluable for disease response, 6/11 (55%) achieved objective responses (2 CRs and 4 PRs); lasting a median of 119 days (range: 48 - 354+).
A Phase 1 Study of Venetoclax (ABT-199 / GDC-0199) Monotherapy in Patients with Relapsed/Refractory Non-Hodgkin Lymphoma


Blood
Volume 126(23):254-254
December 3, 2015
<table>
<thead>
<tr>
<th>Best response on venetoclax, n (%)</th>
<th>DLBCL n=34</th>
<th>DLBCL-RT n=7</th>
<th>Follicular Lymphoma n=29</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response rate (ORR)</td>
<td>5 (15)</td>
<td>3 (43)</td>
<td>10 (34)</td>
</tr>
<tr>
<td>CR</td>
<td>3 (9)</td>
<td>0</td>
<td>3 (10)</td>
</tr>
<tr>
<td>PR</td>
<td>2 (6)</td>
<td>3 (43)</td>
<td>7 (24)</td>
</tr>
<tr>
<td>SD</td>
<td>9 (26)</td>
<td>2 (29)</td>
<td>18 (62)</td>
</tr>
<tr>
<td>PD</td>
<td>18 (53)</td>
<td>1 (14)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Discontinued prior to assessment</td>
<td>1 (3)</td>
<td>1 (14)</td>
<td>0</td>
</tr>
<tr>
<td>Not evaluable</td>
<td>1 (3)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*a Data entry error; response is PR*
Phase I/II, multi-center, single-arm, non-randomized study in which CD30 positive, previously untreated PMBL, DLBCL and grey zone lymphoma (GZL) patients

Novel strategy using combination of brentuximab vedotin, rituximab, cyclophosphamide, doxorubicin and prednisone for a total of 6 cycles

We hypothesize that substituting brentuximab vedotin in place of vincristine in R-CHOP as front-line multi-agent chemotherapy may be well tolerated and improve outcomes in these patients

Phase I completed and established safety/tolerance of 1.8 mg/kg brentuximab vedotin in combination with R-CHP

Phase II evaluates the activity of brentuximab vedotin when administered in combination with multi-agent chemotherapy in patients with CD30 positive PMBL, DLBCL, and GZL
Brentuximab Vedotin in Combination with Multi-Agent Chemotherapy Is Well Tolerated and Shows Promising Activity As Frontline Treatment for Primary Mediastinal B-Cell Lymphoma. Jakub Svoboda, MD et al.
Early Treatment Intensification with R-ICE Chemotherapy Followed By Autologous Stem Cell Transplantation (ASCT) Using Zevalin-BEAM for Patients with Poor Risk Diffuse Large B-Cell Lymphoma (DLBCL) As Identified By Interim PET/CT Scan Performed after Four Cycles of R-CHOP-14: A Multicenter Phase II Study of the Australasian Leukaemia Lymphoma Study Group (ALLG)

by Mark S Hertzberg, Maher K Gandhi, Belinda Butcher, Ruth Columbus, John Taper, Judith Trotman, Devinder Gill, Shir-Jing Ho, Keith Fay, Gavin Cull, Andrew P Grigg, Geoff Chong, Ian D. Lewis, Sam Milliken, William Renwick, Uwe Hahn, Robin Filshie, Anne-Marie Watson, George Kannourakis, Max Wolf, Andrew Wirth, Pauline Therese Warburton, Stephen Robert Larsen, John F. Seymour, and Rodney Hicks

Blood
Volume 126(23):815-815
December 3, 2015

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Progression Free Survival by Interim PET/CT.

Mark S Hertzberg et al. Blood 2015;126:815
Overall survival by Interim PET/CT.

Mark S Hertzberg et al. Blood 2015;126:815
Approaches for the Older Frail patient

Split-dose R-CHOP: A novel approach to administer cytotoxic chemotherapy to geriatric patients with DLBCL
Nirav Shah MD, Nandita Mitra PhD, Joshua Brikman, Sunita Nasta MD, Daniel Landsburg MD, Anthony Mato MD MSCE, Dan Vogl MD, Noelle Frey MD, Steven Schuster MD, Jakub Svoboda MD, AACR 2015
T- cell Lymphomas

- Constitute between 10 and 15 % of all NHL
- What makes T cell lymphomas a challenge?
  - Rarity of the subtypes
  - Biologic heterogeneity
  - Lack of a single effective antibody therapy
  - Relative chemoresistance
Standard of care-PTCL

- CHOP-based on work by the Intergroup trial in the US for intermediate grade lymphomas—mainly with B cell lymphomas
- No clear evidence that more aggressive therapy is helpful in survival though ORR are higher
- Risk stratification may help (IPI and PIT)
- Pathologic/Molecular criteria provide the best clue
  - Treating each subtype based on behavior and molecular characteristics
## Transplant consolidation in PTCL

<table>
<thead>
<tr>
<th>Study</th>
<th>N (enrolled)</th>
<th>N by PTCL subtype</th>
<th>N (TXP)</th>
<th>Median age (years; range)</th>
<th>EFS/PFS (years)</th>
<th>OS (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>d'Amore et al²⁵</td>
<td>160</td>
<td>PTCL-NOS—62</td>
<td>115 (72%)</td>
<td>57 (22-67)</td>
<td>44% (5)</td>
<td>51% (5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AITL—30</td>
<td></td>
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<td></td>
<td></td>
<td>ALCL—31</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Reimer et al¹⁵</td>
<td>83</td>
<td>PTCL-NOS—32</td>
<td>55 (66%)</td>
<td>47 (30-65)</td>
<td>36% (3)</td>
<td>48% (3)</td>
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<tr>
<td></td>
<td></td>
<td>AITL—27</td>
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<td></td>
<td></td>
<td>ALCL—12</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Corradi et al⁵⁶</td>
<td>62</td>
<td>PTCL-NOS—28*</td>
<td>46 (74%)</td>
<td>43 (20-60)</td>
<td>30 (12)</td>
<td>34 (12)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AITL—10</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>ALCL—19†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mehta et al¹³</td>
<td>65‡</td>
<td>PTCL-NOS—32</td>
<td>39 (60%)</td>
<td>58 (22-75)</td>
<td>38% (4)</td>
<td>52% (4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AITL—21</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>ALCL—12</td>
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</tbody>
</table>

April 24, 2014; Blood: 123 (17). How I treat the peripheral T-cell lymphomas, Alison J. Moskowitz¹, Matthew A. Lunning², and Steven M. Horwitz¹
Addition of Etoposide to CHOP Is Associated with Improved Outcome in Adult Anaplastic Large Cell Lymphoma Patients: A Nordic Lymphoma Group Study

- Henrik Cederleuf, Martin Bjerregaard Pedersen, Mats Jerkeman, Thomas Relander, Francesco d'Amore, Fredrik Ellin
- Blood 2015 126:340;
- 371 patients (ALK+ ALCL n=122) --1.3% of all lymphomas
- The median follow-up was 7.2 years. ALK+ patients were younger than ALK- patients (median age 40 versus 66 years, p<0.001).
- The 5-year overall and progression-free survival
  - 78% and 64% in ALK+ ALCL,
  - 37% and 32% in ALK- ALCL
  - 27% and 25% in ALK u ALCL.
# New agents in PTCL

<table>
<thead>
<tr>
<th>Agents</th>
<th>Patients</th>
<th>Central response review</th>
<th>ORR</th>
<th>CR</th>
<th>PFS (months)</th>
<th>DOR (months)</th>
<th>OS (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Romidepsin</td>
<td>130</td>
<td>Yes</td>
<td>25%</td>
<td>15%</td>
<td>4</td>
<td>17</td>
<td>11.3</td>
</tr>
<tr>
<td>Belinostat</td>
<td>129</td>
<td>Yes</td>
<td>26%</td>
<td>10%</td>
<td>NA</td>
<td>8.3</td>
<td>NA</td>
</tr>
<tr>
<td>Pralatrexate</td>
<td>111</td>
<td>Yes</td>
<td>29%</td>
<td>13%</td>
<td>3.5</td>
<td>10.5</td>
<td>14.5</td>
</tr>
<tr>
<td>Bendamustine</td>
<td>60</td>
<td>No</td>
<td>50%</td>
<td>28%</td>
<td>3.6</td>
<td>3.5</td>
<td>6.2</td>
</tr>
<tr>
<td>Brentuximab vedotin</td>
<td>58</td>
<td>Yes</td>
<td>86%</td>
<td>57%</td>
<td>13.3</td>
<td>12.6</td>
<td>NR</td>
</tr>
<tr>
<td>Brentuximab vedotin</td>
<td>34</td>
<td>No</td>
<td>41%</td>
<td>24%</td>
<td>2.6</td>
<td>7.6</td>
<td>NA</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>20</td>
<td>No</td>
<td>55%</td>
<td>30%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>14</td>
<td>No</td>
<td>36%</td>
<td>14%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

PFS, DOR, and OS are all medians in months. DOR, duration of response; NA, not applicable.
First Multicenter, Randomized Phase 3 Study in Patients (Pts) with Relapsed/Refractory (R/R) Peripheral T-Cell Lymphoma (PTCL): Alisertib (MLN8237) Versus Investigator's Choice (Lumiere trial; NCT01482962)

by Owen A. O'Connor, Muhit Özcan, Eric D. Jacobsen, Josep Maria Roncero Vidal, Judith Trotman, Judit Demeter, Tamás Masszi, Juliana Pereira, Radhakrishnan Ramchandren, Francesco A. d'Amore, Francine Foss, Won-Seog Kim, John P. Leonard, Carlos Sérgio Chiattone, Pier Luigi Zinzani, Hua Liu, JungAh Jung, Xiaofei Zhou, E. Jane Leonard, Claudio Dansky Ullmann, and Andrei R. Shustov

Blood
Volume 126(23):341-341
December 3, 2015
## Multicenter Phase II Study of Lenalidomide in Patients with Relapsed Adult T-Cell Leukemia-Lymphoma

Hiroshi Fujiwara, MD PhD et al

<table>
<thead>
<tr>
<th>ATL type</th>
<th>All patients (N = 26)</th>
<th>Acute (n = 15)</th>
<th>Lymphoma (n = 7)</th>
<th>Unfavorable chronic (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR, n (%)</td>
<td>11 (42)</td>
<td>5 (33)</td>
<td>4 (57)</td>
<td>2 (50)</td>
</tr>
<tr>
<td>CR/CRu, n (%)</td>
<td>5 (19)</td>
<td>3 (20)</td>
<td>2 (29)</td>
<td>0</td>
</tr>
<tr>
<td>PR, n (%)</td>
<td>6 (23)</td>
<td>2 (13)</td>
<td>2 (29)</td>
<td>2 (50)</td>
</tr>
<tr>
<td>SD, n (%)</td>
<td>8 (31)</td>
<td>6 (40)</td>
<td>0</td>
<td>2 (50)</td>
</tr>
<tr>
<td>PD, n (%)</td>
<td>7 (27)</td>
<td>4 (27)</td>
<td>3 (43)</td>
<td>0</td>
</tr>
</tbody>
</table>

- CR, complete response; CRu, CR unconfirmed; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.
Risk-Adapted Therapy in Adults with Burkitt Lymphoma: Preliminary Report of a Multicenter Prospective Phase II Study of DA-EPOCH-R


Blood
Volume 126(23):342-342
December 3, 2015

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Progression Free Survival by LR or HR

Kieron Dunleavy et al. Blood 2015;126:342
Long Term Outcomes of Rituximab, High-Dose Methotrexate and Temozolamide Regimen for Diffuse Large B-Cell for Lymphomas Involving the Central Nervous System Sarah J. Nagle, MD, et al Blood 126(3) ASH 2015

- 46 patients with primary or secondary CNS DLBCL
  - RMT at our institution between January 2009 and December 2014.
  - The median age at diagnosis was 61 years (range 21-85 years).
  - Twenty-seven (59%) patients had primary CNS DLBCL and 19 (41%) patients had secondary CNS DLBCL. Twenty-six (57%) patients had a CR to therapy, 6 (14%) patients had a partial response (PR), 4 (9%) patients had stable disease (SD) and 10 (22%) patients had PD. The overall response rate was 70%.
- Median OS was 41 months. Median PFS was 7 months.
- Patients who received 2 or fewer cycles of RTM had a significantly shorter OS as compared with those who received 3 or more cycles of RTM (3 months vs. NR; p<0.0001).
- Compared with secondary CNS DLBCL, patients with primary CNS DLBCL had a significantly longer OS (54 months vs. 5 months; p=0.0074).
Overall Survival RTM Regimen
DA-TEDDI-R (temozolomide, etoposide, doxil, dexamethasone, ibrutinib and rituximab) (with intraventricular cytarabine). Methotrexate was excluded due to potential antagonism with ibrutinib based on preliminary in vitro experiments.

11 patients enrolled; 6 were R/R (median 3 (1-5) prior treatments) and 5 were previously untreated. Eleven completed the ibrutinib window and 5 patients completed and 2 remain on DA-TEDDI-R; Ibrutinib dosing was 560 mg in patients 1-6; 700 mg in patients 7-10; and 840 mg in patient 11. There were 3 on-study deaths: from progressive disease, infection and ventricular arrhythmia.

With ibrutinib alone, 7 of 8 evaluable patients achieved partial responses, and 1 patient had a mixed response. After DA-TEDDI-R, all 5 patients achieved complete remission of which 4 (all R/R) are in remission at 1+, 2+, 3+, and 6+ months, and 1 (previously untreated) patient relapsed at 3 months.