Welcome
Case Studies in Rare Lymphomas
Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

Program Objective/Description
A case-based discussion about the management of the patient with Hodgkin lymphoma following failure of autologous stem cell transplant; the patient with relapsed and refractory Hodgkin lymphoma; and the patient with systemic anaplastic large cell lymphoma following failure of one or more combination regimens.

Supported by an independent grant from

Produced by

Case Studies in Rare Lymphomas
Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

Moderator
James O. Armitage, MD
Professor, Department of Internal Medicine
Joe Shapiro Distinguished Chair of Oncology
University of Nebraska Medical Center
Omaha, Nebraska

Faculty
Joseph M. Connors, MD, Clinical Director, Centre for Lymphoid Cancer, British Columbia Cancer Agency, University of British Columbia, Vancouver, British Columbia
Andreas Engert, MD, Chairman, German Hodgkin Study Group, Professor for Internal Medicine, University Hospital of Cologne, Cologne, Germany
Steven M. Horwitz, MD, Assistant Attending, Lymphoma Service, Memorial Sloan-Kettering Cancer Center, New York, New York

Program recorded July 16, 2012
Copyright 2012 by Harborside Press, LLC
## Case Studies in Rare Lymphomas: Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

### Disclosures of Potential Conflicts of Interest

**James O. Armitage, MD:** Consultant or Advisory Role: Ziopharm, Seattle Genetics, Genetics, Allos, Roche  
**Joseph M. Connors, MD:** Institutional research support, including clinical trials: Amgen, Bayer Healthcare, Cephalon, Genentech, Hoffmann-LaRoche, Johnson & Johnson, Lilly, Merck, Roche Canada, Seattle Genetics  
**Andreas Engert, MD:** Research support/honoraria, Millennium, Takeda  
**Steven Horwitz, MD:** Grant/research: Celgene, Allos, Seattle Genetics; consultant: Celgene, Allos, Seattle Genetics, Bristol-Myers Squibb, Genzyme, Kyowa, Hakko Kirin, Johnson & Johnson

---

### Case Studies in Rare Lymphomas  
**Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma**

**Moderator**  
James O. Armitage, MD  
Professor; Department of Internal Medicine  
Joe Shapiro Distinguished Chair of Oncology  
University of Nebraska Medical Center  
Omaha, Nebraska

**Program**

**Management of a Patient with Hodgkin Lymphoma Following Failure of Autologous Stem Cell Transplant**  
Joseph M. Connors, MD, British Columbia Cancer Agency Centre for Lymphoid Cancer, University of British Columbia

**Management of a Patient with Relapsed and Refractory Hodgkin Lymphoma**  
Andreas Engert, MD, German Hodgkin Lymphoma Study Group, University of Cologne, Cologne, Germany

**Management of a Patient with Systemic Anaplastic Large Cell Lymphoma Following Failure of One or More Combination Regimens**  
Steven M. Horwitz, MD, Memorial Sloan-Kettering Cancer Center, New York, New York

---

### Welcome

Case Studies in Rare Lymphomas  
Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

**Program Objective/Description**

A case-based discussion about the management of the patient with Hodgkin lymphoma following failure of autologous stem cell transplant; the patient with relapsed and refractory Hodgkin lymphoma; and the patient with systemic anaplastic large cell lymphoma following failure of one or more combination regimens.

Supported by an independent grant from Seattle Genetics

Produced by ASCO "Post"
Multiple-choice Questions

1. Would you classify yourself as an academic- or a community-based health care professional?
2. Are you office- or hospital-based?
3. How many years have you been in practice?
4. How many new patients do you treat with lymphoma each month?

Management of a Patient with Hodgkin Lymphoma Following Failure of Autologous Stem Cell Transplant

Joseph M. Connors, MD
Clinical Director, Centre for Lymphoid Cancer
British Columbia Cancer Agency
University of British Columbia
Vancouver, British Columbia

Hodgkin Lymphoma Relapse After Autologous Stem Cell Transplant

- 26-year-old male with stage III B nodular sclerosing Hodgkin lymphoma
- ABVD x 6 => PET negative CR
- 4 months later, relapse in neck & mediastinum
- GDP x 2 + high-dose BEAM + auto-SCT => PET negative CR
- 6 months later, relapse in neck & mediastinum

Node-only relapse in patient with never irradiated original node-only disease
Hodgkin Lymphoma
Relapse After Autologous Stem Cell Transplant

- 26-year-old male with stage III B nodular sclerosing Hodgkin lymphoma
- ABVD x 6 => PR, PET positive neck & mediastinum => IFRT => PET negative CR
- 9 months later, relapse in neck & mediastinum
- GDP x 2 + high dose BEAM + auto-SCT => PET negative CR
- 9 months later, relapse in neck & mediastinum
- ESHAP x 2 => PET negative CR

Chemosensitive late relapse (> 6 months after autologous stem cell transplant)
NOT primary progressor on ABVD

Typical patient with relapse after autologous stem cell transplant

HDC/RT + auto-SCT FOR HL
Refractory vs Relapsed

~ 40% of patients who undergo autologous stem cell transplant for Hodgkin lymphoma relapse again
Case Studies in Rare Lymphomas:
Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

Prognosis for HL Patients who Relapse After Autologous Stem Cell Transplant

72% of patients who relapse do so in the first 12 months after ASCT

1-year mortality 40%

TTR = Time to relapse.
Horning, et al. 10th International Conference on Malignant Lymphoma; Lugano, Switzerland; 2008.

HDC/RT + auto-SCT FOR HL
Overall Survival after Relapse after SCT

Cumulative Survival

Treatment Options for Hodgkin Lymphoma in Relapse After Autologous Stem Cell Transplant

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Frequency</th>
<th>Treatment</th>
<th>Cure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Node-only relapse in patient</td>
<td>5% to 10%</td>
<td>Extended-field radiation</td>
<td>50%</td>
</tr>
<tr>
<td>with never irradiated original node-only disease</td>
<td></td>
<td>+/- MOPP-type chemoTx</td>
<td></td>
</tr>
</tbody>
</table>
**Case Studies in Rare Lymphomas:**

**Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma**

### Treatment Options for Hodgkin Lymphoma in Relapse After Autologous Stem Cell Transplant

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Frequency</th>
<th>Treatment</th>
<th>Cure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Node-only relapse in patient</td>
<td>5% to 10% with never irradiated original</td>
<td>Extended-field radiation +/- MOPP-type chemoTx</td>
<td>50%</td>
</tr>
<tr>
<td>Chemo-sensitive late relapse (&gt; 6 months after auto-SCT)</td>
<td>10% to 20%</td>
<td>Allo-SCT on a clinical trial</td>
<td>??% (&lt; 40%)</td>
</tr>
<tr>
<td>NOT primary progressor on ABVD</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

Overall and progression free survival after allogeneic stem-cell transplantation (alloSCT) for Hodgkin lymphoma according to the type of conditioning regimen.

---

**Figure:** Cumulative survival after relapse after SCT.

- **Alive:** 24
- **Alive w/o lymphoma:** 11
- **All 11 received, as their last treatment:**
  - **RT alone:** 7
  - **RT + chemoTx:** 4

**HDC/RT + auto-SCT FOR HL**

**Overall Survival after Relapse after SCT**

- **Survival:**
  - 1.0
  - 0.9
  - 0.8
  - 0.7
  - 0.6
  - 0.5
  - 0.4
  - 0.3
  - 0.2
  - 0.1
  - 0.0

**Post SCT Survival (y)**

- **Cumulative Survival:**
  - **RT alone:** 7
  - **RT + chemoTx:** 4

---

**Reference:**

Case Studies in Rare Lymphomas: Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

### Treatment Options for Hodgkin Lymphoma in Relapse after Auto-SCT

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Frequency</th>
<th>Treatment</th>
<th>Cure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Node-only relapse in patient</td>
<td>5% to 10%</td>
<td>Extended-field radiation</td>
<td>50%</td>
</tr>
<tr>
<td>with never irradiated original node-only disease</td>
<td></td>
<td>+/- MOPP-type chemoTx</td>
<td></td>
</tr>
<tr>
<td>Chemo-sensitive late relapse</td>
<td>10% to 20%</td>
<td>Allo-SCT on a clinical trial</td>
<td>??? (&lt;40%)</td>
</tr>
<tr>
<td>(&gt; 6 months after auto-SCT)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOT primary progressor on ABVD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All other patients</td>
<td>70% to 80%</td>
<td>Single agent chemoTx</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+/- involved field RT</td>
<td></td>
</tr>
</tbody>
</table>

### Treatment Options for Hodgkin Lymphoma in Relapse after Autologous Stem Cell Transplant

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Frequency</th>
<th>Treatment</th>
<th>Cure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>All other patients</td>
<td>70% to 80%</td>
<td>Single-agent chemoTx</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+/- involved field RT</td>
<td></td>
</tr>
</tbody>
</table>

### Single agent chemoTx options

<table>
<thead>
<tr>
<th>Agent</th>
<th>ORR</th>
<th>CR</th>
<th>Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vinblastine</td>
<td>~60%</td>
<td></td>
<td>Few months</td>
<td>IV 1-2 weekly, little toxicity</td>
</tr>
<tr>
<td>Lomustine</td>
<td>~50%</td>
<td></td>
<td>Few months</td>
<td>Oral, q 6-8 weeks, myelotoxic</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>~40%</td>
<td></td>
<td>Few months</td>
<td>IV weekly, little Sx toxicity, myelotoxic</td>
</tr>
<tr>
<td>Bendamustine</td>
<td>~70%</td>
<td></td>
<td>Few months</td>
<td>IV, q 3-4 weeks, marked myelotoxic, very little experience/data</td>
</tr>
<tr>
<td>Brentuximab</td>
<td>~75%</td>
<td>35%</td>
<td>&gt; 6 to 12 mo</td>
<td>IV, modest neuropathy, very well tolerated, excellent evidence base</td>
</tr>
</tbody>
</table>

### Management of a Patient with Hodgkin Lymphoma Following Failure of Autologous Stem Cell Transplant

Panel Discussion

James O. Armitage, MD  Joseph M. Connors, MD  Andreas Engert, MD  Steven M. Horowitz, MD
Case Studies in Rare Lymphomas: Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

Management of a Patient with Relapsed and Refractory Hodgkin Lymphoma

Andreas Engert, MD
Chairman, German Hodgkin Study Group
Professor for Internal Medicine
Hematology and Oncology
University Hospital of Cologne
Department of Internal Medicine
Cologne, Germany

R&R Hodgkin Lymphoma Case Report

- 23-year-old female patient
- Diagnosed with Hodgkin lymphoma January 2009
- 2x ABVD (1-3/09): PD
- 2x BEACOPPesc (3-5/09): PR

Primary Progressive Hodgkin Disease
1988-1998 (German Hodgkin Study Group)

OS and FF2F for All Patients (n = 206)

Case Studies in Rare Lymphomas:
Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

Relapsed Hodgkin Lymphoma Overview

- 23-year-old female patient
- Diagnosed with Hodgkin lymphoma Jan 2009
- 2x ABVD (1-3/09): PD
- 2x BEACOPPesc (3-5/09): PR
- 1x ICE (6/09): PD
- 2x DHAP (7-8/09)
- BEAM + ABMT (9/09)
- Radiotherapy 12/09 – 2/10
- PD in 5/10

Brentuximab Vedotin (SGN-35)
Mechanism of Action

- Brentuximab vedotin (SGN-35) ADC
  - monomethyl auristatin E (MMAE), potent antitubulin agent
  - protease-cleavable linker
  - anti-CD30 monoclonal antibody

ADC binds to CD30
ADC-CD30 complex traffics to lysosome
MMAE is released
G2/M cell cycle arrest
Apoptosis

Phase II of SGN-35 (Brentuximab Vedotin)
Maximum Reduction in Target Lesions

94% (96 of 102) of patients achieved tumor reduction

Individual patients (n=98*)

Case Studies in Rare Lymphomas: Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

Brentuximab Vedotin Representative Case
(23-year-old female relapsed and refractory Hodgkin lymphoma)

Pre Brentuximab vedotin
After 4 Cycles

Relapsed and Refractory Hodgkin Lymphoma Summary

- 23-year old female patient with relapsed and refractory Hodgkin lymphoma
- Received 4 lines of chemo, HDCT and RT
- Still progressive disease
- CR after 4 cycles of brentuximab vedotin and proceeded to allogeneic stem cell transplant
- Anti-CD30 ADC brentuximab vedotin registered for relapsed and refractory Hodgkin lymphoma since 8-11
- Brentuximab vedotin associated with 75% RR; (34%) CR in pivotal trial
- Major side effects (WHO grade III/IV) neutropenia (20%) and neuropathy (9%)

Management of a Patient with Relapsed and Refractory Hodgkin Lymphoma

Panel Discussion
Management of a Patient with Systemic Anaplastic Large Cell Lymphoma (ALCL) Following Failure of One or More Combination Regimens

Steven M. Horwitz, MD
Assistant Attending
Lymphoma Service
Memorial Sloan-Kettering Cancer Center
New York, New York

49-Year-Old Woman Referred with a New Diagnosis of ALCL

- Right axillary lymphadenopathy
- Present for 2-3 months, slow growth,
- Excisional biopsy

Right Axillary Lymph Node

CD30
CD4
H&E
ALK-1
Case Studies in Rare Lymphomas: Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

PET-CT Shows Subpectoral and Lung Involvement

FNA Lung Nodule

49-Year-Old Woman Referred with a Diagnosis of ALK- ALCL

- BM negative
- LDH elevated
- IPI 2 (Stage IV, LDH)
- Recommended to receive CHOEP + ASCT
Case Studies in Rare Lymphomas: Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

**Anaplastic Large Cell Lymphoma, OS by ALK Status and IPI**

OS: ALK+ vs ALK-

<table>
<thead>
<tr>
<th>ALK+</th>
<th>ALK-</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS</td>
<td>OS</td>
</tr>
<tr>
<td>&lt; .01</td>
<td>&lt; .01</td>
</tr>
</tbody>
</table>


**CHOEP +/- ASCT if PTCL**

- **CHOEP: EFS**
  - Younger, NL LDH

- **CHOEP-14 x 6 + ASCT: EFS**
  - ALCL
  - AITL
  - PTCL

D’Amore, et al. ASH 2011 (JCO in press)

**49-Year-Old Woman Referred with a Diagnosis of ALK-, ALCL**

- Has a CR to CHOEP
- Receives ASCT
- Does well
- Repeat scans 1 year after ASCT-new LAN
- Biopsy shows recurrent ALCL
Case Studies in Rare Lymphomas:
Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>ORR</th>
<th>PFS months</th>
<th>DR</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pralatrexate</td>
<td>109</td>
<td>29%</td>
<td>3.5</td>
<td>10.1</td>
<td>FDA approved</td>
</tr>
<tr>
<td>Romidepsin</td>
<td>130</td>
<td>25%</td>
<td>4</td>
<td>17</td>
<td>FDA approved</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>39</td>
<td>51%</td>
<td></td>
<td></td>
<td>CTCL + PTCL</td>
</tr>
<tr>
<td>Bendamustine</td>
<td>60</td>
<td>50%</td>
<td>3.5</td>
<td></td>
<td>Preliminary</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>39</td>
<td>51%</td>
<td>3.5</td>
<td></td>
<td>Preliminary</td>
</tr>
<tr>
<td>Camidanoside</td>
<td>23</td>
<td>30%</td>
<td>3</td>
<td></td>
<td>Allowed newly diagnosed</td>
</tr>
</tbody>
</table>


Brentuximab Vedotin

Brentuximab Vedotin (SGN-35) ADC
- monomethyl auristatin E (MMAE), potent antitubulin agent
- protease-cleavable linker
- anti-CD30 monoclonal antibody

ADC binds to CD30
ADC-CD30 complex traffics to lysosome
MMAE is released
MMAE disrupts microtubule network
G2/M cell cycle arrest
Apoptosis

Brentuximab Vedotin in Relapsed ALCL

<table>
<thead>
<tr>
<th>Measure</th>
<th>Response (N = 58)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective response rate, %</td>
<td>85</td>
<td>74.6 to 90.3</td>
</tr>
<tr>
<td>OR rate</td>
<td>57</td>
<td>43.2 to 69.3</td>
</tr>
<tr>
<td>Partial remission rate</td>
<td>29</td>
<td>19.3 to 39.0</td>
</tr>
<tr>
<td>Stable disease, %</td>
<td>3</td>
<td>0 to 10.8</td>
</tr>
<tr>
<td>Progressive disease, %</td>
<td>5</td>
<td>0 to 10.8</td>
</tr>
<tr>
<td>Histologically ineligible, %</td>
<td>3</td>
<td>0 to 10.8</td>
</tr>
<tr>
<td>Not evaluable, %</td>
<td>2</td>
<td>0 to 10.8</td>
</tr>
<tr>
<td>Median duration of objective response, months</td>
<td>12.6</td>
<td>5.7 to NE</td>
</tr>
<tr>
<td>Median duration of response in patients with CR, months</td>
<td>13.2</td>
<td>10.8 to NE</td>
</tr>
<tr>
<td>Median progression-free survival, months</td>
<td>13.3</td>
<td>6.9 to NE</td>
</tr>
<tr>
<td>Median overall survival, months</td>
<td>Not reached</td>
<td>14.8 to NE</td>
</tr>
</tbody>
</table>

Case Studies in Rare Lymphomas:
Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

Brentuximab Vedotin in Relapsed ALCL

Brentuximab Vedotin in Relapsed ALCL: PFS

Brentuximab Vedotin in Relapsed ALCL: Toxicities

Case Studies in Rare Lymphomas: Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

Romidepsin and Pralatrexate: Response Analysis by Subsets

<table>
<thead>
<tr>
<th></th>
<th>PTCL-NOS (n = 69)</th>
<th>AITL (n = 27)</th>
<th>ALK-1–Negative ALCL (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Romidepsin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Best Response, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORR</td>
<td>19 (28)</td>
<td>9 (33)</td>
<td>5 (24)</td>
</tr>
<tr>
<td>CR</td>
<td>11 (17)</td>
<td>7 (26)</td>
<td>4 (19)</td>
</tr>
<tr>
<td>PR</td>
<td>8 (12)</td>
<td>2 (7)</td>
<td>1 (5)</td>
</tr>
<tr>
<td><strong>Pralatrexate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Patients</td>
<td>59</td>
<td>13</td>
<td>17</td>
</tr>
<tr>
<td>Proportion of Patients</td>
<td>54%</td>
<td>12%</td>
<td>16%</td>
</tr>
<tr>
<td>ORR</td>
<td>32%</td>
<td>8%</td>
<td>35%</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• PTCL-NOS</td>
<td>59</td>
<td>13</td>
<td>17</td>
</tr>
<tr>
<td>• AITL</td>
<td>12</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>• ALCL</td>
<td></td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>• Transformed MF</td>
<td></td>
<td>12</td>
<td>16</td>
</tr>
</tbody>
</table>


49-Year-Old Woman Referred With a Diagnosis of ALK-, ALCL

- Has a PR to brentuximab vedotin
- Refer for allogeneic stem cell transplant

Retrospective Analyses of Allogeneic Stem-cell Transplantation for PTCL

Management of a Patient with Systemic Anaplastic Large Cell Lymphoma (ALCL) Following Failure of One or More Combination Regimens

Panel Discussion

Thank You for Your Attention

Moderator
James O. Armitage, MD

Faculty
Joseph Connors, MD, Andreas Engert, MD, and Steven Horwitz, MD

This program is also available in a print and digital edition. For more information, e-mail editor@ASCOPost.com or visit www.ASCOPost.com.

Thank you for participating in this webcast on Case Studies in Rare Lymphomas: Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

Supported by an independent grant from Seattle Genetics

Produced for ASCO POST

This program is also available in a print and digital edition. For more information, e-mail editor@ASCOPost.com or visit www.ASCOPost.com.