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

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

SeattleGenetics

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THE ASCO POST

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

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Faculty

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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 18, 2012

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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

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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

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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

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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

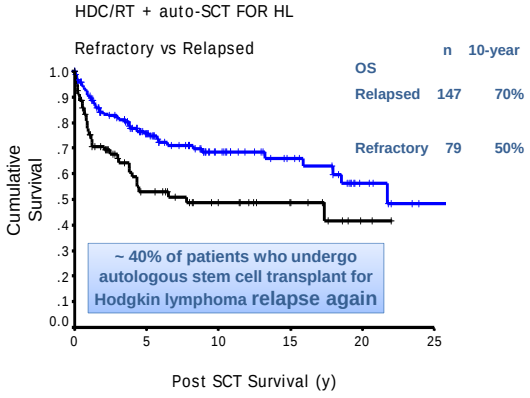
Chemosensitive late relapse
(> 6 months after autologous stem cell transplant)
NOT primary progressor on ABVD

Hodgkin Lymphoma

Relapse After Autologous Stem Cell Transplant

- 26-year-old male with stage II B bulky nodular sclerosing Hodgkin lymphoma
- **ABVD => progression during cycle 5**
- GDP x 2 + high dose BEAM + auto-SCT + IFRT (neck & mediastinum) => PET negative CR
- 4 months later, relapse in neck & mediastinum

Typical patient with relapse after autologous stem cell transplant



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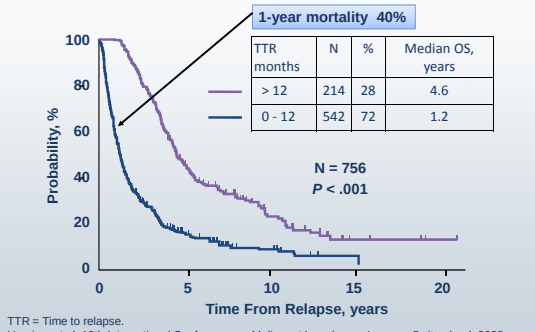
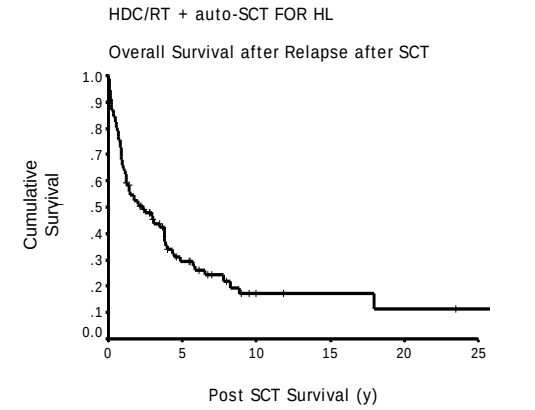
Prognosis for HL Patients who Relapse After Autologous Stem Cell Transplant

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



TTR = Time to relapse.

Horning, et al. 10th International Conference on Malignant Lymphoma; Lugano, Switzerland; 2008.



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

Patient Group	Frequency	Treatment	Cure Rate
Node-only relapse in patient with never irradiated original node-only disease	5% to 10 %	Extended-field radiation +/- MOPP-type chemoTx	50%

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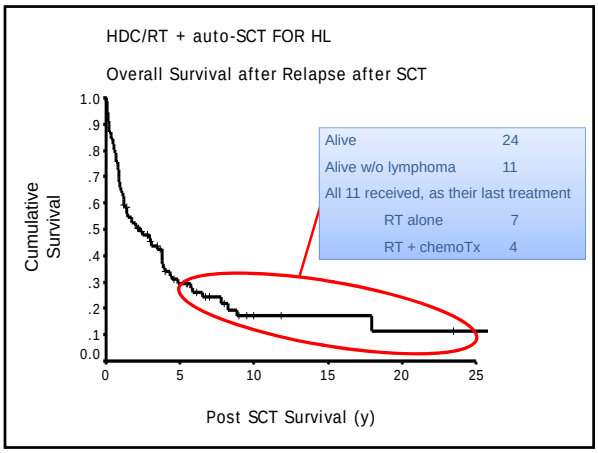

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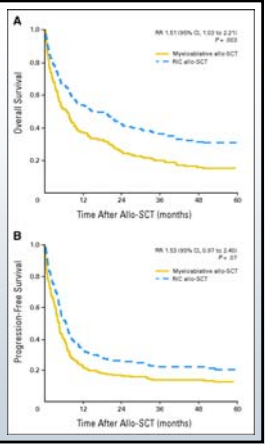
Patient Group	Frequency	Treatment	Cure Rate
Node-only relapse in patient with never irradiated original node-only disease	5% to 10%	Extended-field radiation +/- MOPP-type chemoTx	50%
Chemo-sensitive late relapse (> 6 months after auto-SCT) NOT primary progressor on ABVD	10% to 20%	Allo-SCT on a clinical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

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



Sureda, A. et al. *J Clin Oncol*. 2008;26:455-462.

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

Treatment Options for Hodgkin Lymphoma in Relapse after Auto-SCT

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

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

All other patients	70% to 80%	Single-agent chemoTx +/- involved field RT	None

Single agent chemoTx options

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

Management of a Patient with Hodgkin Lymphoma Following Failure of Autologous Stem Cell Transplant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Andreas Engert, MD


Steven M. Horwitz, MD

Panel Discussion

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

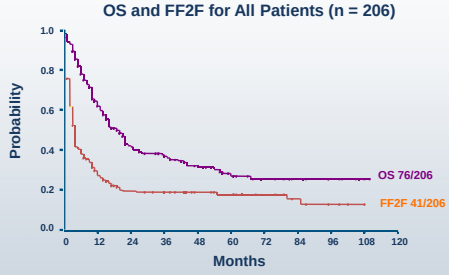
R&R Hodgkin Lymphoma Case Report

- 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)



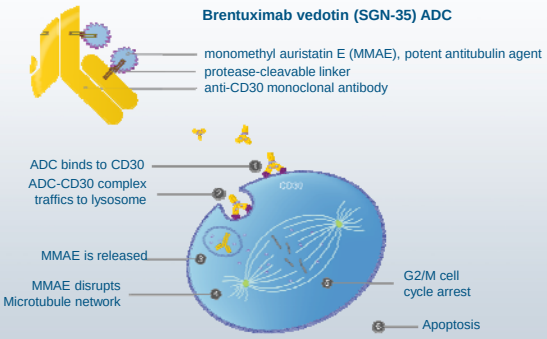
Abbreviations: FF2F, freedom from second treatment failure; OS, overall survival.
Josting A, et al. *Blood.* 2000;96(4):1280-1286.

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

Relapsed Hodgkin Lymphoma Overview

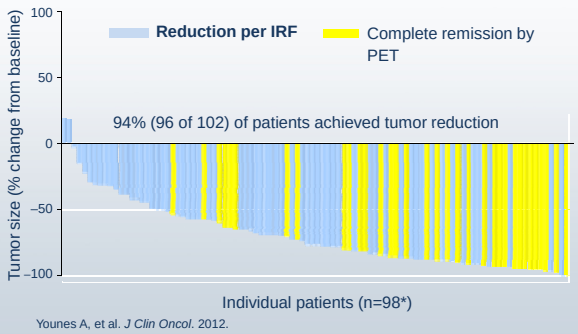
- 23-year-old female patient
- Diagnosed with Hodgkin lymphoma Jan 2009
- 2x ABVD (1-3/09): PD
- 2x BEACOPPesc (3-5/09): PR
- 1x ICE (6/09); PD
- 2x DHAP (7-8/09)
- BEAM + ABMT (9/09)
- Radiotherapy 12/09 – 2/10
- PD in 5/10

Brentuximab Vedotin (SGN-35) Mechanism of Action



Phase II of SGN-35 (Brentuximab Vedotin)

Maximum Reduction in Target Lesions



Younes A, et al. *J Clin Oncol*. 2012.

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^{o} III/IV) neutropenia (20%) and neuropathy (9%)

Management of a Patient with Relapsed and Refractory Hodgkin Lymphoma

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Panel Discussion

Case Studies in Rare Lymphomas:
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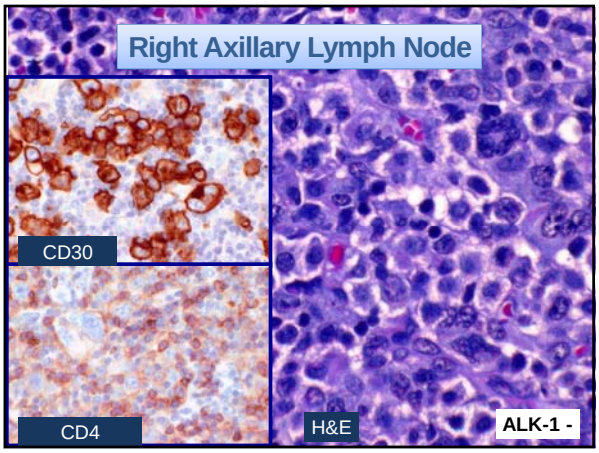
Management of a Patient with Systemic Anaplastic Large Cell Lymphoma (ALCL) Following Failure of One or More Combination Regimens

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

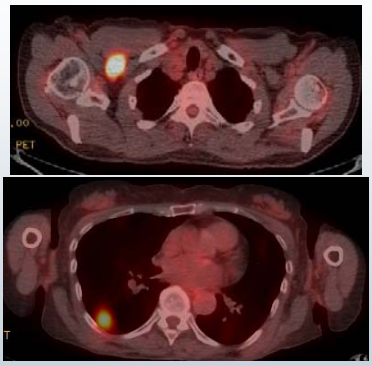
49-Year-Old Woman Referred with a New Diagnosis of ALCL

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

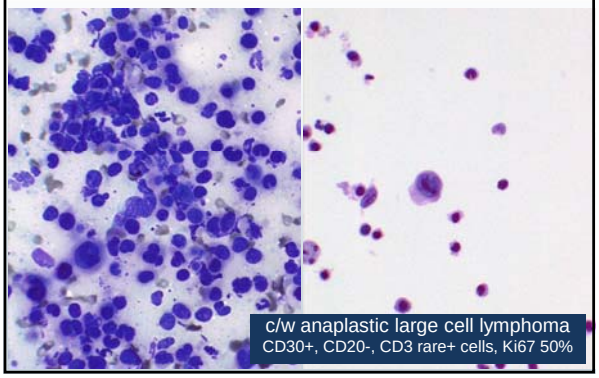


Case Studies in Rare Lymphomas: Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

PET-CT Shows Subpectoral and Lung Involvement



FNA Lung Nodule

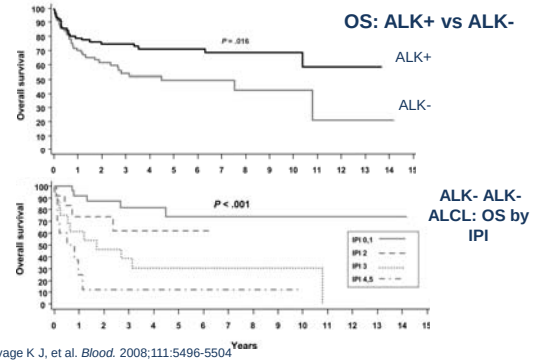


49-Year-Old Woman Referred with a Diagnosis of ALK-, ALCL

- BM negative
- LDH elevated
- IPI 2 (Stage IV, LDH)
- Recommended to receive CHOEP +ASCT

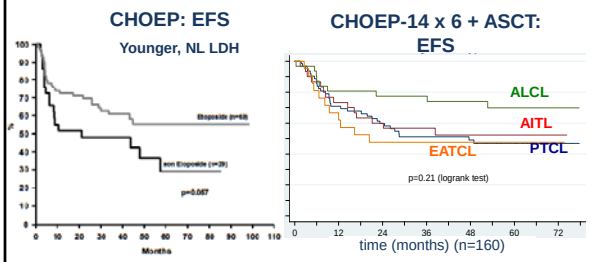
Case Studies in Rare Lymphomas: Hodgkin Lymphoma and Systemic Anaplastic Large Cell Lymphoma

Anaplastic Large Cell Lymphoma, OS by ALK Status and IPI



Savage K J, et al. *Blood.* 2008;111:5496-5504

CHOEP +/- ASCT if PTCL



Schmitz, et al. *Blood.* 2010;116(18):3418-3425.
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:
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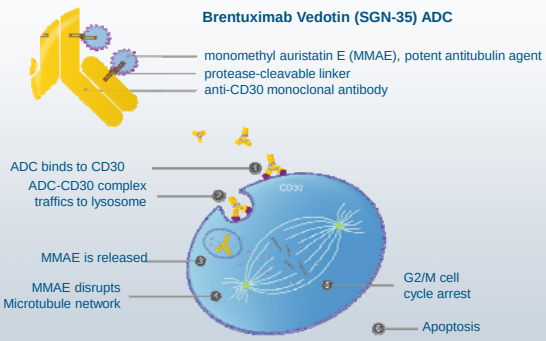
Studies of Relapsed/Refractory PTCL

Treatment	N	ORR	PFS months	DR	Comments
Pralatrexate	109	29%	3.5	10.1	FDA approved
Romidepsin	130	25%	4	17	FDA approved
Gemcitabine	39	51%			CTCL + PTCL
Bendamustine	60	50%		3.5	Preliminary
Lenalidomide	23	30%	3		Allowed newly diagnosed

O'Conner ,OA, et al. *J Clin Oncol.* 2011;29:1182-1189.
Coiffier B, et al. *J Clin Oncol*. 2012; Epub
Zinzani PL, et al. *Ann Oncol*. 2010;21:860-863.
Damaj G, et al. ASCO 2012 .
Dueck, et al. *Cancer*. 2010;116(19):4541-4548.

Brentuximab Vedotin



Brentuximab Vedotin in Relapsed ALCL

Measure	Response (N = 58)	95% CI
Objective response rate, %	86	74.6 to 93.9
CR rate*	57	43.2 to 69.8
Partial remission rate	29	
Stable disease, %	3	
Progressive disease, %	5	
Histologically ineligible, %†	3	
Not evaluable, %	2	
Median duration of objective response, months	12.6	5.7 to NE
Median duration of response in patients with CR, months	13.2	10.8 to NE
Median progression-free survival, months	13.3	6.9 to NE
Median overall survival, months	Not reached	14.6 to NE

Pro B, et al. *J Clin Oncol*. 2012;30:2190-2196.

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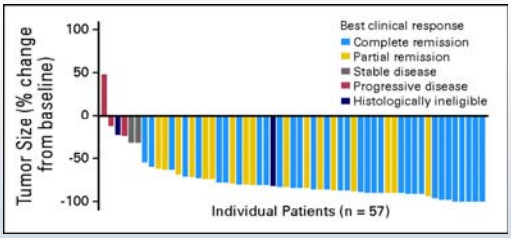
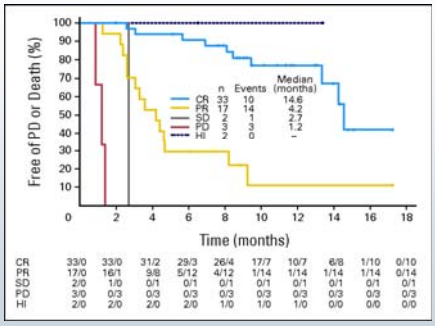
Brentuximab Vedotin in Relapsed ALCL



Pro B, et al. *J Clin Oncol*. 2012;30:2190-2196.

Brentuximab Vedotin in Relapsed ALCL: PFS



Pro B, et al. *J Clin Oncol*. 2012;30:2190-2196.

Brentuximab Vedotin in Relapsed ALCL: Toxicities

Adverse Event*	All Grades (N = 58)		Grade 3 (N = 58)		Grade 4 (N = 58)	
	No. of Patients	%	No. of Patients	%	No. of Patients	%
Peripheral sensory neuropathy	24	41	7	12	0	0
Nausea	23	40	1	2	0	0
Fatigue	22	38	2	3	1	2
Pyrexia	20	34	1	2	0	0
Diarrhea	17	29	2	3	0	0
Rash	14	24	0	0	0	0
Constipation	13	22	1	2	0	0
Neutropenia	12	21	7	12	5	9

Pro B, et al. *J Clin Oncol*. 2012;30:2190-2196.

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Romidepsin and Pralatrexate: Response Analysis by Subsets

Romidepsin			
Best Response, n (%)	PTCL-NOS (n = 69)	AITL (n = 27)	ALK-1–Negative ALCL (n = 21)
ORR	19 (28)	9 (33)	5 (24)
CR	11 (17)	7 (26)	4 (19)
PR	8 (12)	2 (7)	1 (5)

Pralatrexate	Number of Patients	Proportion of Patients	ORR
Histology			
• PTCL-NOS	59	54%	32%
• AILT	13	12%	8%
• ALCL	17	16%	35%
• Transformed MF	12	11%	25%

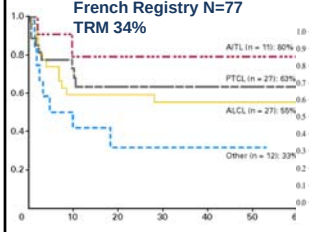
O'Conner OA, et al. *J Clin Oncol.* 2011;29:1182-1189.

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

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

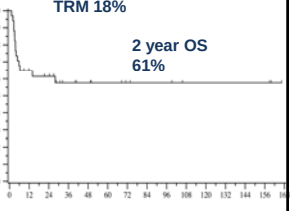
Retrospective Analyses of Allogeneic Stem-cell Transplantation for PTCL

French Registry N=77
TRM 34%



MSKCC N=34
TRM 18%

2 year OS
61%



Le Gouill S, et al. *J Clin Oncol.* 2008;26:2264-2271 .
Goldberg J, et al. *Leuk Lymphoma.* 2012 Jan 31 Epub.

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Panel Discussion

Thank You for Your Attention

Moderator
James O. Armitage, MD

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

Thank you for participating in this webcast on

Case Studies in Rare Lymphomas

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