5 Minute JournalClub

POST-ASH Issue 6, 2014

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CME Information

LEARNING OBJECTIVES

- Evaluate the benefits and risks of brentuximab vedotin after long-term follow-up of patients with relapsed or refractory Hodgkin lymphoma.
- Assess the efficacy and safety of brentuximab vedotin in investigational settings, such as for elderly and pediatric patients with Hodgkin lymphoma or as salvage therapy prior to stem cell transplant.
- Appraise recent clinical trial data on the use of panobinostat in combination with chemotherapy for relapsed or refractory Hodgkin lymphoma.
- Recall the clinical features, treatment, survival outcomes and prognosis of gray zone lymphoma.

CME Information (Continued)

CREDIT DESIGNATION STATEMENT
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FACULTY DISCLOSURES
The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

CME Information (Continued)

Andrew M Evens, DO, MSc
Professor of Medicine
Chief, Division of Hematology/Oncology
Tufts University School of Medicine
Director, Lymphoma Program
Leader, Clinical Sciences Program
Tufts Cancer Center
Boston, Massachusetts

Advisory Committee and Contracted Research: Celgene Corporation, Millennium: The Takeda Oncology Company, Seattle Genetics.

Christopher Flowers, MD, MS
Associate Professor of Hematology and Medical Oncology
Emory School of Medicine Winship Cancer Institute
Atlanta, Georgia

Advisory Committee: Biogen Idec, Genentech BioOncology, Roche Laboratories Inc; *Consulting Agreements:* Algeta ASA, Celgene Corporation, OptumRx Inc; *Contracted Research:* Abbott Laboratories, Celgene Corporation, Millennium: The Takeda Oncology Company, Spectrum Pharmaceuticals Inc.

CME Information (Continued)

Craig Moskowitz, MD
Clinical Director, Division of Hematologic Oncology
Attending Physician, Lymphoma and Adult BMT Services
Member, Memorial Sloan-Kettering Cancer Center
Professor of Medicine, Weill Medical College of Cornell University
New York, New York

Advisory Committee: GlaxoSmithKline, Roche Laboratories Inc, Seattle Genetics; *Contracted Research:* Cephalon Inc, GlaxoSmithKline, Roche Laboratories Inc, Seattle Genetics; *Paid Research:* Plexxikon Inc.

5 MinuteJournalClub

POST-ASH Issue 6, 2014

One of the best ways to allow experienced clinical investigators to illustrate their perspectives on the translation of research to clinical care is to ask them to present and discuss patients from their practices, and this month in Miami and New York we will do just that by hosting daylong CME symposia structured around 32 cases managed by 10 invited researchers (Join us! Click here). In reviewing the first faculty slide set submitted for the Miami meeting by Dr Craig Moskowitz, I was immediately drawn to his selection of a case of a 72-year-old woman with classical Hodgkin lymphoma (cHL) who had significant comorbidities requiring a plethora of medications. The dilemma of this important cHL subset — which is estimated to comprise up to 35% of cHL patients — is that the natural history of the disease seems somewhat more aggressive, yet poor health and reduced baseline renal function often mean that even modified chemotherapy regimens may not be delivered at close to full doses.

Dr Moskowitz includes in his talk a slide illustrating the design of a single-arm Phase II trial in older patients evaluating the antibody-drug conjugate brentuximab vedotin (bv) followed by scaled back chemotherapy (AVD [doxorubicin/vinblastine/dacarbazine]) and then bv consolidation. This is not the first time we have heard about this intriguing study, as last summer at our

lymphoma think tank Dr Andrew Evens presented an 87-year-old woman who had entered the trial but unfortunately had major problems with the chemotherapy during the first cycle, including sepsis and congestive heart failure.

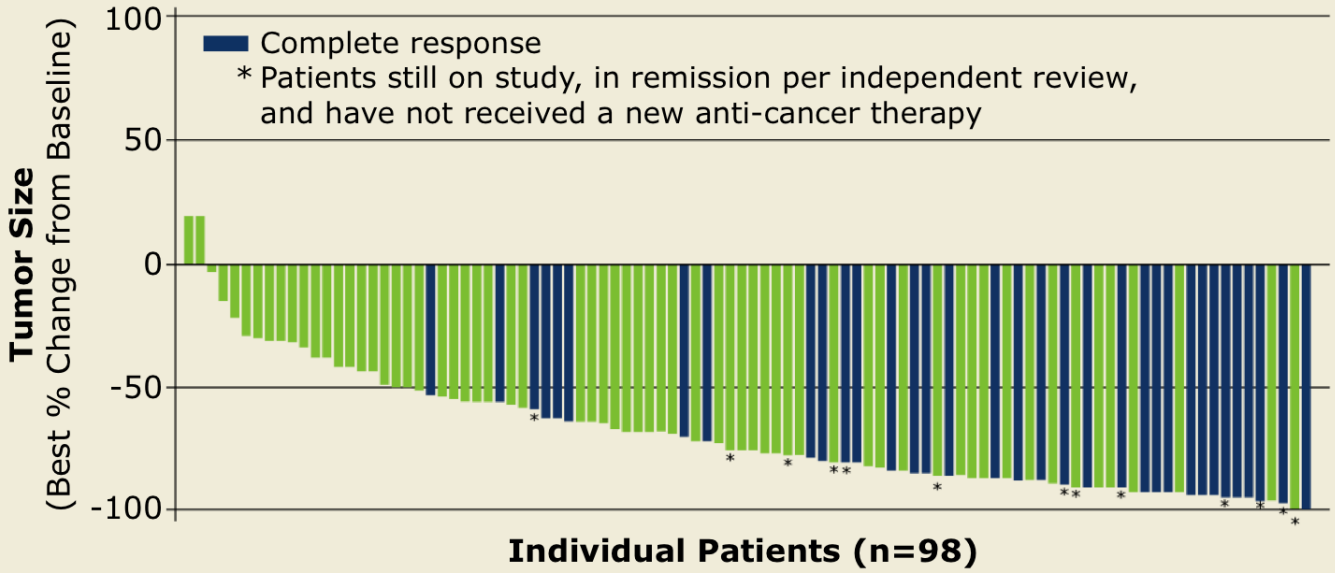
For precisely this reason many clinicians have for some time expressed great interest in taking things even further and eliminating chemotherapy altogether for the "frail elderly" population, and at ASH we got a first glimpse that this in fact may be quite possible. Specifically, preliminary data were presented from 11 of the projected 50 patients aged 60 and older enrolled on **an ongoing Phase II study** of bv up front. The results were impressive, as 7 patients achieved a complete response (CR) and 2 had a partial response. Among these, the 2 that got my attention were a 92-year-old woman with Stage IV disease and PS 1 and an 88-year-old man with Stage II disease and PS 2, both of whom had CRs. It is worth noting that the durability of these responses in this very early data set has not yet been established, and it could be, as is being tested in the trial discussed at the think tank, that integration of some form of chemotherapy will be optimal.

The challenge of the frail elderly patient permeates all corners of oncology, and oncologists frequently inquire about the potential up front role of agents like T-DM1 in HER2-positive breast cancer or ibrutinib in CLL and mantle-cell lymphoma as less toxic alternatives when even "gentle" forms of chemotherapy like paclitaxel and bendamustine pose a significant risk. I will be curious to find out in Miami what happened with Dr Moskowitz's 72-year-old patient and to hear his thoughts and those of the other faculty members on how this compelling issue plays out in their practices as well as their perspectives on new HL data sets presented in New Orleans, including those profiled below:

- **More follow-up of bv in relapsed/refractory (RR) HL**

The **3-year update** from the pivotal Phase II study revealed a median overall survival of 40.5 months with 14 of the 76 patients who had objective responses still in remission, suggesting that a fraction of these patients may be cured. Perhaps even more impressive, the waterfall plot (see below) illustrates that all but 2 of the 98 patients experienced decreases in tumor size, and 34 patients (35%) achieved CR.

Responses in a Phase II Trial of Brentuximab Vedotin in Relapsed/Refractory Hodgkin Lymphoma



- Patients received a median of 9 cycles (range, 1–16) of B-vedotin
- Those who achieved an objective response received more cycles of therapy

With permission from Gopal AK et al. *Proc ASH* 2013;Abstract 4382.

On the flip side of the coin, while bv is generally better tolerated than conventional chemotherapy, toxicities are a reality, and almost half of the patients in this study experienced some form of neuropathy (only 9% being Grade 3 or 4). In a related matter, an interesting ASH poster described 8 cases of pancreatitis in patients receiving bv, including 2 who died of that complication. Although this rare but concerning side effect has been reported with other tubulin drugs, it is of interest that CD30 is present on normal pancreatic cells, but it is not clear if this is of clinical significance with regard to this phenomenon. Regardless, many investigators caution that a baseline serum amylase and lipase should be obtained and that abdominal discomfort be investigated thoroughly.

In New Orleans we were also treated to **a fascinating report** from Memorial Sloan-Kettering on the use of bv prior to autotransplant. This Phase II study demonstrated that in 11 of 42 patients (26%), bv resulted in FDG PET-negative scans, allowing patients to proceed to transplant without more chemotherapy. This appealing strategy seems likely to be considered for nonprotocol therapy in the future. Finally, **a Phase I/II study** reported encouraging response and tolerability findings using bv in 16 pediatric patients with HL.

- **Phase I study of panobinostat combined with ICE (ifosfamide/ carboplatin/etoposide) in RR cHL**

The subject of novel agents in HL was addressed at ASH in a brilliant review lecture by Dr Anas Younes. In addition to other monoclonal antibodies and antibody-drug conjugates, he highlighted histone deacetylase inhibitors and

agents targeting the PI3 kinase pathways as ones to look out for. In that regard, in New Orleans we saw **data from a Phase I study** evaluating panobinostat combined with ICE. The regimen resulted in CR in 15 of 21 (71%) patients, and all were able to have stem cells harvested successfully, with 17 responding patients going on to autotransplant without additional treatment except mobilization chemotherapy. Toxicity was considered "acceptable" and included fatigue, GI complaints and myelosuppression, but of course Phase III testing will be needed to determine the potential additional benefit of this regimen.

- **Gray zone lymphoma case series**

Dr Evens and colleagues **reported a retrospective analysis** of 96 patients diagnosed with this difficult-to-classify B-cell lymphoma that commonly has features intermediate between primary mediastinal diffuse large B-cell lymphoma (DLBCL) and cHL. This important paper identified a subset of these patients who present without mediastinal involvement and have distinct characteristics. Patients in this series received various forms of chemotherapy and, in most cases, rituximab, and overall the outcomes seem less favorable than with either DLBCL or cHL. At a median follow-up of 25 months, 2-year progression-free survival is 41% and overall survival is 84%, suggesting that much more research is needed to optimize the care of these patients.

- **Reduced-intensity conditioning for allotransplant for RR HL in the "bv era"**

Allotransplant is thought to have the potential to eradicate HL via a graft-versus-host effect, and **this retrospective report** of 27 patients suggested

better outcomes among patients who had received prior bv. The findings, while preliminary, appear to have renewed interest in allotransplant for HL.

Next, on the final issue of our ASH review series, we visit perhaps the most exciting corner of the field — chimeric antigen receptor T-cell therapy, as discussed by an investigator in the middle of it all, Dr David Porter.

Neil Love, MD
Research To Practice
Miami, Florida

A Phase 2 Study of Single-Agent Brentuximab Vedotin for Front-Line Therapy of Hodgkin Lymphoma in Patients Age 60 Years and Above: Interim Results

Yasenchak CA et al.

Proc ASH 2013;Abstract 4389.

Background

- Patients who are aged ≥60 years with Hodgkin lymphoma have disproportionately inferior outcomes compared to younger patients.
- Comorbidities in older patients are associated with higher rates of treatment-related toxicities and can prevent delivery of the standard intensity and/or duration of chemotherapy (*Blood* 2012;119:692).
- A retrospective analysis of patients aged ≥60 years with relapsed/refractory CD30+ lymphomas across 7 single-agent brentuximab vedotin studies showed antitumor activity and durable responses consistent with those observed in younger patients (*Leuk Lymphoma* 2013;[Epub ahead of print]).
- **Study objective:** To conduct an interim analysis of efficacy and safety of front-line brentuximab vedotin monotherapy for patients with HL who are ≥60 years of age.

Yasenchak CA et al. *Proc ASH* 2013;Abstract 4389.

Ongoing Phase II Trial Design

NCT01716806

Target accrual (n = 50)*

Classical HL (Stages I-IV)
Previously untreated
Age ≥60 years
ECOG PS ≤3
Ineligible for or declined conventional chemotherapy

Brentuximab vedotin
1.8 mg/kg (IV)
Every 3 weeks

Patients achieving stable disease (SD) or better can receive up to 16 cycles of treatment, after which therapy can be continued for those experiencing clinical benefit.

* To date, 13 patients have been enrolled

- **Primary endpoint:** Objective response rate (ORR)
- Response assessments are performed at cycles 2, 4, 8, 12 and at the end of treatment (EOT)
  - This includes PET scans at cycles 2, 8 and EOT

Yasenchak CA et al. *Proc ASH* 2013;Abstract 4389; www.clinicaltrials.gov, accessed February 2014.

Baseline Characteristics

Characteristic	n = 13
Median age (range)	75 years (64-92)
Male	54%
With moderate age-related renal insufficiency (CrCl ≥30 and <60 mL/min)	54%

CrCl = creatinine clearance

Yasenchak CA et al. *Proc ASH* 2013;Abstract 4389 (abstract only).

Responses

Response rate	n = 11
ORR	82%
Complete response (CR)	64%
Partial response (PR)	18%
Patients with interim PET scans after 2 cycles of therapy	**n = 10**
Mean decrease in SUVmax from baseline	83%
Patients with negative scans at cycle 2*	36%

SUVmax = maximum standardized uptake value

* To date, range of duration of response: 0.1+ to 20.6+ weeks

- To date, patients have received a median of 5 cycles of therapy
  - Range: 1-11

Yasenchak CA et al. *Proc ASH* 2013;Abstract 4389 (abstract only).

Best Response Type by Patient

Patient	Age/sex	Dx Stage*	ECOG PS	Response
1	70 y/F	IV	1	CR†
2	79 y/F	II	1	SD
3	92 y/F	IV	1	CR
4	78 y/M	II	1	CR
5	64 y/M	I	0	CR
6	67 y/M	II	0	PR†
7	88 y/M	II	2	CR†
8	75 y/M	III	1	PR†
9	71 y/F	II	0	CR†
10	74 y/F	II	1	SD†
11	78 y/M	IV	1	CR†

* Disease stage at diagnosis; † Still on treatment

Yasenchak CA et al. *Proc ASH* 2013;Abstract 4389 (abstract only).

Reasons for Study Discontinuation

- Patients discontinued treatment (n = 4):
  - Due to progressive disease (n = 2)
  - Due to a serious adverse event (n = 1)
    - Grade 3 orthostatic hypotension
  - Due to patient decision (n = 1)

Yasenchak CA et al. *Proc ASH* 2013;Abstract 4389 (abstract only).

Adverse Events

- Treatment-related adverse events occurring in ≥15% of patients included:
  - Decreased neutrophil count (n = 2)
  - Peripheral sensory neuropathy (n = 2)
  - Pruritus (n = 2)
  - Rash (n = 2)
- Most adverse events were Grade 1 or 2.
- Grade 3 treatment-related adverse events included:
  - Decreased neutrophil count (n = 1)
  - Rash (n = 1)
  - Orthostatic hypotension (n = 1)
- No Grade 4 or 5 adverse events have been observed to date.

Yasenchak CA et al. *Proc ASH* 2013;Abstract 4389 (abstract only).

Author Conclusions

- In this interim analysis of patients aged ≥60 years with newly diagnosed HL, compelling antitumor activity with single-agent brentuximab vedotin was demonstrated.
- To date, a response rate of 82% has been shown in this historically challenging population of patients who either declined or were ineligible for standard chemotherapy.
- Preliminary safety data demonstrated tolerability in this patient population, and the data are consistent with the current safety profile of brentuximab vedotin.

Yasenchak CA et al. *Proc ASH* 2013;Abstract 4389 (abstract only).

Investigator Commentary: Interim Analysis of an Ongoing Single-Arm Phase II Trial of Up-Front Brentuximab Vedotin (B-Vedotin) Monotherapy for Patients Aged ≥60 Years with HL

This is an interesting study. The term "elderly" sometimes bears a negative connotation. However, HL is a more malignant, virulent disease in older patients. We know that we find much more mixed cellularity in this setting. With the elderly, we see more Epstein-Barr virus-related and advanced-stage disease than we see in younger patients.

This Phase II study showed a respectable response rate with single-agent B-vedotin without chemotherapy. Usually, responses with B-vedotin in HL are quick, within about 2 cycles. The critical question about this study is, will this be a durable response? Although B-vedotin is a type of chemotherapy, it's more of an antitubulin-like agent. I would argue that the most important agent is an alkylator such as dacarbazine and the second most important therapy is an anthracycline. Therefore, I am not surprised about the initial response rate but the crucial question is, can it be maintained? Will relapses occur because of the lack of an alkylating or chemotherapeutic agent? We will need to see those data. Even so, this would be an attractive treatment strategy for older patients who cannot tolerate any chemotherapy.

Interview with Andrew M Evens, DO, MSc, February 12, 2014

Three-Year Follow-Up Data and Characterization of Long-Term Remissions from an Ongoing Phase 2 Study of Brentuximab Vedotin in Patients with Relapsed or Refractory Hodgkin Lymphoma

Gopal AK et al.

Proc ASH 2013;Abstract 4382.

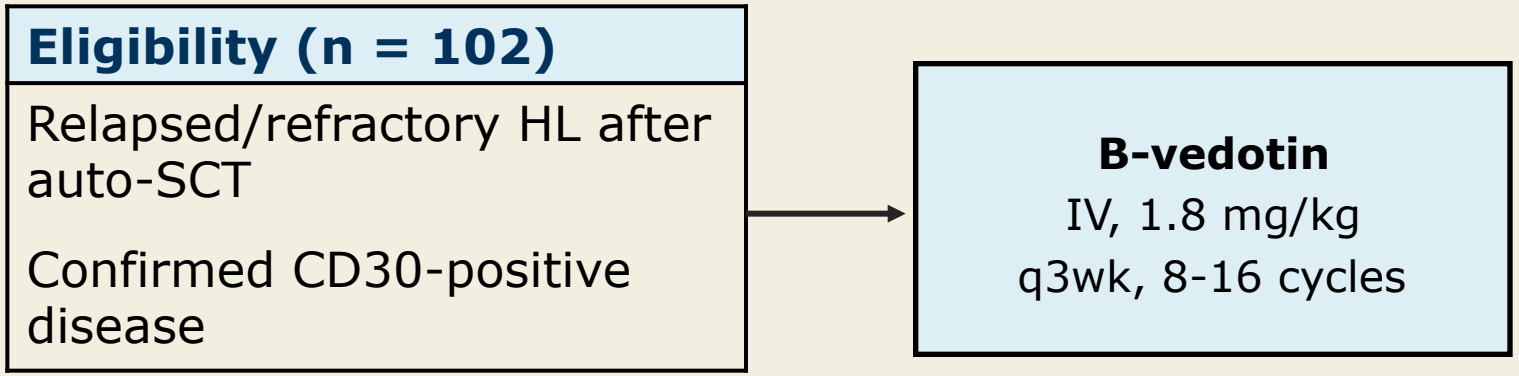
Background

- The standard treatment for patients with relapsed or refractory Hodgkin lymphoma (HL) is salvage chemotherapy followed by autologous stem cell transplant (auto-SCT).
- However, approximately 50% of patients experience relapse of HL after auto-SCT, and this population represents a pronounced unmet need.
- A pivotal Phase II study demonstrated an overall response rate of 75% with complete remission (CR) in 34% of patients with relapsed/refractory HL treated with brentuximab vedotin (B-vedotin) after auto-SCT (*JCO* 2012;30:2183-9).
- **Study objective:** To present 3-year follow-up data from this Phase II study on the efficacy and safety of B-vedotin for relapsed or refractory HL.

Gopal AK et al. *Proc ASH* 2013;Abstract 4382.

Ongoing Phase II Study Design

NCT00848926

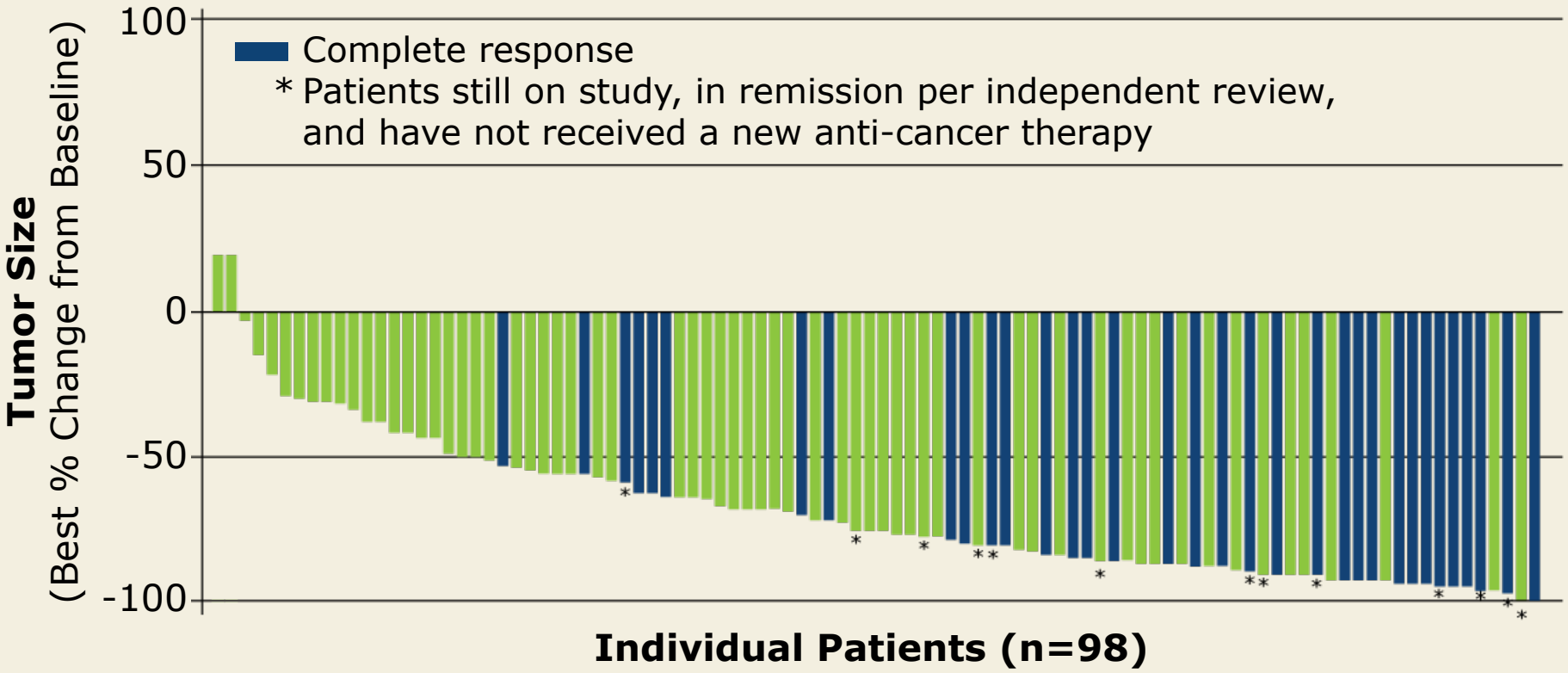


Primary endpoint: Objective response rate per independent review facility

Secondary endpoints include: CR rate, progression-free survival (PFS), overall survival and safety.

Gopal AK et al. *Proc ASH* 2013;Abstract 4382.

Response by Central Independent Review



- Patients received a median of 9 cycles (range, 1–16) of B-vedotin
- Those who achieved an objective response received more cycles of therapy

With permission from Gopal AK et al. *Proc ASH* 2013;Abstract 4382.

Survival Outcomes

- The median overall survival was 40.5 months.
- The estimated 3-year survival rate was 54%.
- At a median of 32.7 months since first dose of B-vedotin, 51 of 102 patients (50%) were alive at the time of last follow-up.
- The median PFS by central independent review was 5.6 months.
  - 76 patients achieved CR/partial response: median PFS = 9 months
  - 26 patients experienced stable/progressive disease: median PFS = 2.8 months

Gopal AK et al. *Proc ASH* 2013;Abstract 4382.

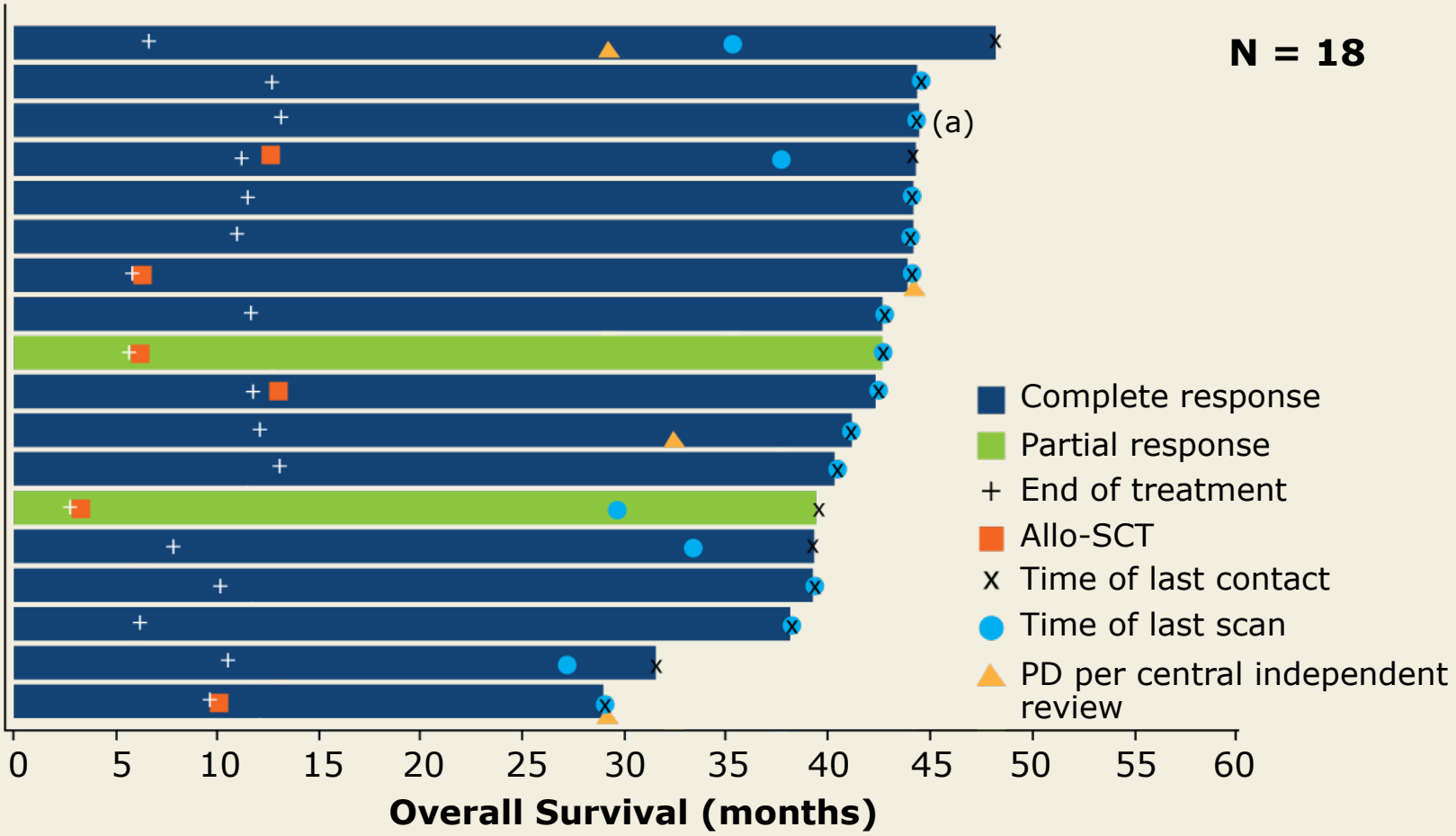
Characterization of Long-Term Remissions by Central Independent Review

Characteristic	Still in remission and on study (N = 14)	With objective response but no longer in remission* (N= 62)	Non-responders (N = 26)
Demographics and baseline disease characteristics			
Median age (range)	26.5 (15-54)	32.0 (18-77)	35.0 (18-70)
Median number prior therapies (range)	2.5 (2-7)	3.0 (1-13)	4.0 (2-8)
Median time (mo) from auto-SCT to relapse (range)	7.8 (2-33)	7.3 (1-131)	5.2 (0-41)
Median PFS (wk) from last prior therapy	25.1	27.7	21.1
Exposure and safety information			
Median number of cycles (range)	13.5 (4-16)	9.5 (3-16)	7.0 (1-16)
Patients with Grade ≥3 AEs, n (%)	9 (64)	32 (52)	15 (58)
Patients with AE of peripheral neuropathy, n (%)	9 (64)	36 (58)	11 (42)

* Includes patients still on study for survival follow-up who have experienced disease progression or initiation of new therapy and patients who have discontinued study treatment for reasons including death, loss to follow-up, withdrawal of consent and physician decision

Gopal AK et al. *Proc ASH* 2013;Abstract 4382.

Long-Term Remissions by Investigator Review



[a] Allo-SCT information unknown

- 18 patients who remain in remission are being followed on study

With permission from Gopal AK et al. *Proc ASH* 2013;Abstract 4382.

Select Adverse Events (≥20%)

Adverse event	All grades	Grade 3/4
Peripheral sensory neuropathy	47%	9%
Fatigue	46%	2%
Nausea	42%	—
Upper respiratory tract infection	37%	—
Diarrhea	36%	1%
Pyrexia	29%	2%
Neutropenia	22%	20%

Other Grade 3/4 events in ≥5% of patients: thrombocytopenia (8%) and anemia (6%)

Gopal AK et al. *Proc ASH* 2013;Abstract 4382.

Author Conclusions

- After a median observation time of approximately 3 years from the first dose of B-vedotin, 50% of patients with relapsed or refractory HL were alive at the time of last follow-up.
  - Median overall survival was 40.5 months.
- Eighteen patients remain in remission per investigator review, and 14 of these patients remain in remission per central independent review.
  - This provides an early suggestion that a fraction of these patients may be cured.
- A randomized Phase III study is being conducted to evaluate B-vedotin in combination with AVD versus ABVD (doxorubicin, bleomycin, vinblastine and dacarbazine) for front-line treatment of advanced classical HL (NCT01712490).

Gopal AK et al. *Proc ASH* 2013;Abstract 4382.

Investigator Commentary: Ongoing Phase II Study of B-Vedotin in Relapsed/Refractory HL — 3-Year Follow-Up and Characterization of Long-Term Remissions

This was a 3-year follow-up study of the pivotal trial of B-vedotin in patients with relapsed/refractory HL after an auto-SCT. The study reported a high overall response rate of 75%. Half of the patients were alive with a median overall survival of 40.5 months. This suggests that for patients who experience a response to B-vedotin after failure of auto-SCT, the responses are durable.

The standard approach for patients with relapsed/refractory HL is salvage chemotherapy followed by stem cell transplant. B-vedotin is usually administered after auto-SCT and is a good option for these patients.

In terms of the side effects of B-vedotin, neurologic toxicity is one that all physicians should be aware of. Pneumonitis is of particular concern for patients with HL because they may have received other agents like bleomycin that can cause overlapping toxicity. B-vedotin has also been associated with pancreatitis, and dermatologic problems may occur occasionally.

Interview with Christopher Flowers, MD, MS, February 24, 2014

FDG-PET Adapted Sequential Therapy with Brentuximab Vedotin and Augmented ICE Followed by Autologous Stem Cell Transplant for Relapsed and Refractory Hodgkin Lymphoma

Moskowitz A et al.

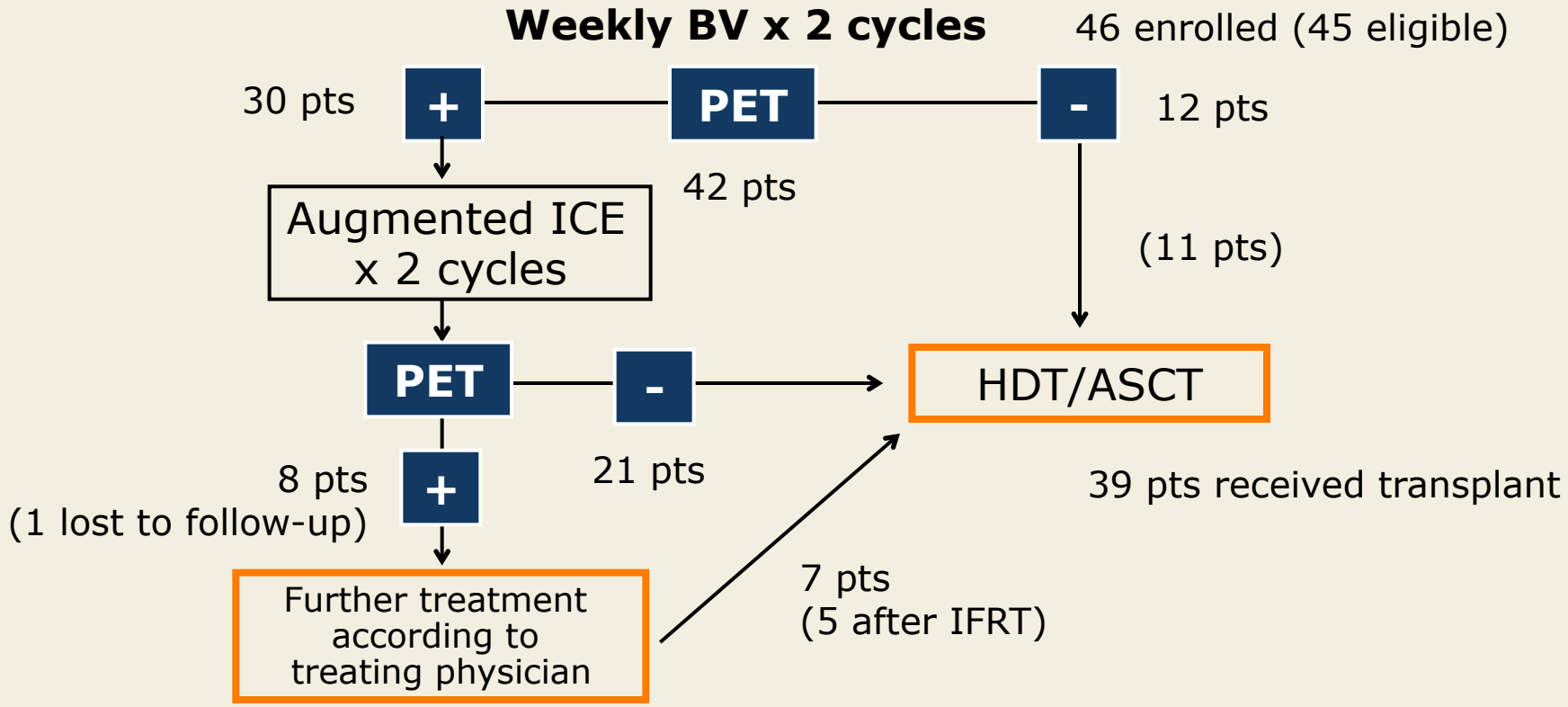
Proc ASH 2013;Abstract 2099.

Background

- Pretransplant ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) normalization is the strongest predictor of outcome after autologous stem cell transplant (ASCT) for patients with relapsed or refractory Hodgkin lymphoma (HL) (*Blood* 2010;116:4934).
- Brentuximab vedotin (BV) has demonstrated high efficacy in patients for whom ASCT has failed.
- **Study objective:** To determine whether BV can replace ICE (ifosfamide/carboplatin/ etoposide) salvage therapy, increase the rate of PET normalization and enhance referral to ASCT among patients with HL after the failure of front-line therapy.

Moskowitz A et al. *Proc ASH* 2013;Abstract 2099.

Phase II Trial Design



HDT = high-dose therapy; IFRT = involved-field radiation therapy

- Disease status before ASCT:
  - Deauville 2, 34 patients (2 after IFRT)
  - Partial response after IFRT, 3 patients
  - Deauville 3, 2 patients

Moskowitz A et al. *Proc ASH* 2013;Abstract 2099.

Patient Characteristics

Characteristic	N = 42
Median age (range)	31 years (13-65)
Initial disease stage I II III IV	 2% 48% 21% 29%
Stage at enrollment II III IV	 45% 14% 40%
Relapse after initial Tx: >1 year/≤1 year	17%/33%
Primary refractory disease	50%
Extranodal disease	43%
Presence of B symptoms	31%

Moskowitz A et al. *Proc ASH* 2013;Abstract 2099.

Transplant Characteristics

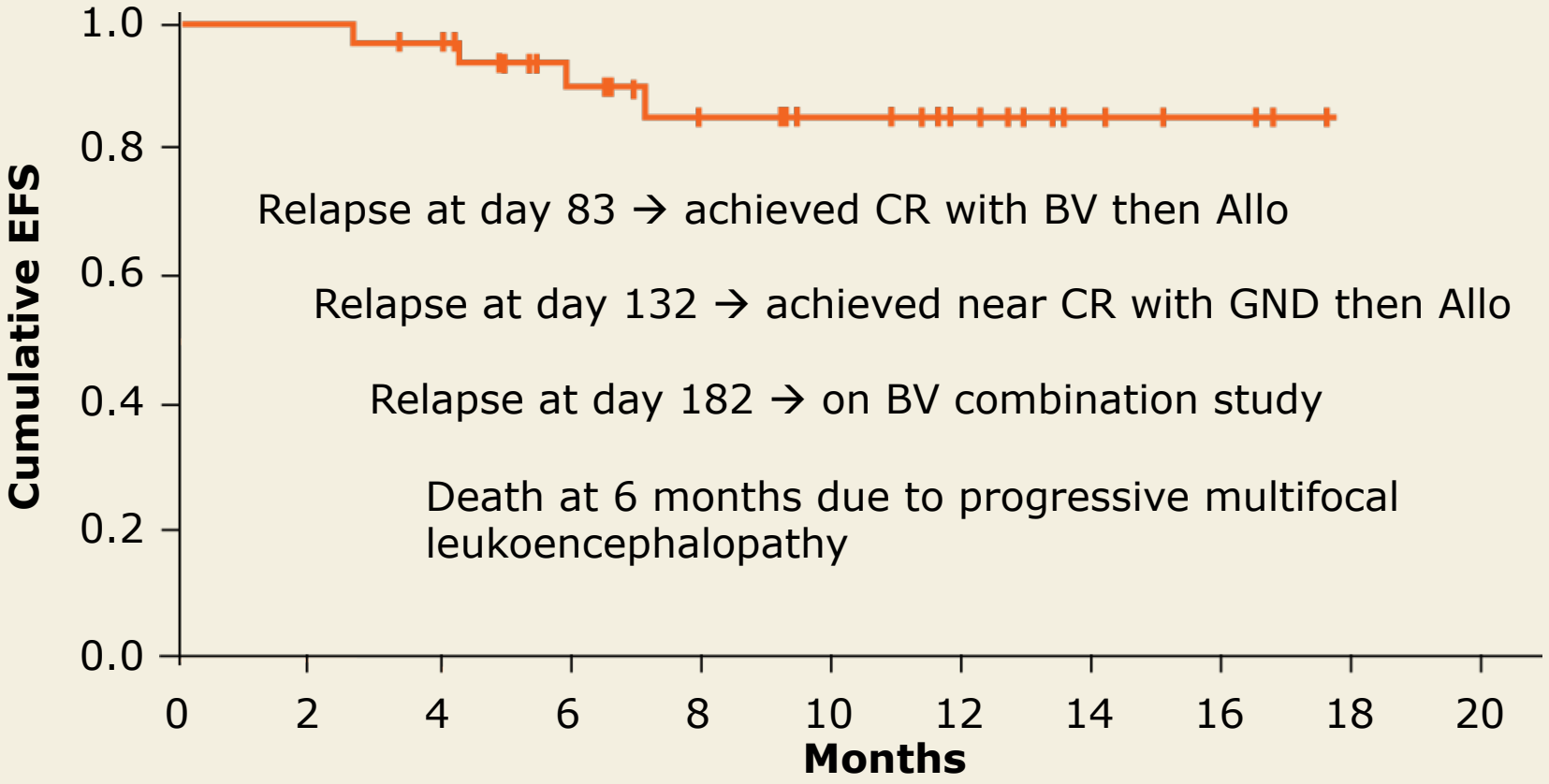
Stem cell collection	Median (range), million/kg
BV alone	6.28 (2.96-13.29)
BV → augmented ICE	9.41 (4.56-31.43)

Conditioning regimen	N = 39
Hyperfractionated IFRT → CBV or BEAM	3
Hyperfractionated IFRT → TLI/CV	7
IFRT → CBV or BEAM	5
CBV or BEAM	24

C = cyclophosphamide; B = carmustine; V = etoposide; BEAM = carmustine/etoposide/cytarabine/melphalan; TLI = total lymphoid irradiation

Moskowitz A et al. *Proc ASH* 2013;Abstract 2099.

Event-Free Survival (EFS)



Median follow-up from transplant: 10 months

- CR = complete response; Allo = allogeneic stem cell transplant; GND = gemcitabine/vinorelbine/doxorubicin

With permission from Moskowitz A et al. *Proc ASH* 2013;Abstract 2099.

Select Salvage-Related Adverse Events (AEs) (N = 42)

BV-related AEs	Grade 1	Grade 2	Grade 3
Neuropathy	40%	14%	0%
Rash	55%	14%	2%

Augmented ICE-related serious AEs	Grade 3 or 4
Febrile neutropenia	43%
Vomiting	2%
Bone pain	2%
Sepsis	2%
Anemia	2%
Thrombocytopenia	2%
Anorectal infection	2%

Moskowitz A et al. *Proc ASH* 2013;Abstract 2099.

Transplant-Related Morbidity (N = 39)

Early	No. of patients	Status
Pneumonitis	3	Resolved
Neuropathy (Grade 3)	1	Ongoing
Acute kidney injury	1	Resolved
Late	**No. of patients**	**Status**
Pneumonitis	1	Resolved
Esophagitis	1	Underwent dilatation
Chronic renal failure	1	Ongoing
PML	1	Death

PML = progressive multifocal leukoencephalopathy

Moskowitz A et al. *Proc ASH* 2013;Abstract 2099.

Author Conclusions

- PET-adapted sequential salvage therapy with BV with or without augmented ICE:
  - Produces high rates of PET normalization
    - 79% Deauville 2, 83% Deauville 2 or 3
  - Facilitates referral to ASCT for virtually all patients
    - 93% of evaluable patients have undergone transplant
  - Is associated with manageable toxicity and adequate stem cell collection
- With short (median 10 months) follow-up, 92% of patients who underwent transplant are progression free.
- This treatment strategy is a reasonable approach for transplant-eligible patients with relapsed/refractory HL and provides a platform for testing novel BV combinations.

Moskowitz A et al. *Proc ASH* 2013;Abstract 2099.

Investigator Commentary: FDG-PET-Adapted Sequential Treatment with BV and Augmented ICE → ASCT in Relapsed/Refractory HL

BV is the best drug I've ever seen in HL, and I would say that most experts would agree. Currently, single-agent BV is not approved for patients after first relapse. In this study, we administered BV on a weekly basis as opposed to the label dose, which is every 3 weeks. Patients received weekly BV on a 3 weeks on, 1 week off schedule for 2 cycles, followed by a repeat PET scan. This is novel because if the PET scans were negative, patients did not receive any salvage chemotherapy. Stem cells were collected from the patients before they underwent transplant. This study attempts to reduce treatment prior to stem cell transplant (SCT). Preliminary data that we presented at Lugano showed that the sequential treatment was remarkable — about 80% of patients were in remission at the time of transplant (*Proc ICML* 2013;Abstract 141).

There are a variety of reasons for this approach. I'm convinced that salvage chemotherapy causes infertility and many other problems that we observe. Changing the management of advanced HL with a novel drug is unique. Although the cost of BV is an issue, if BV has the capacity to markedly improve clinical outcome, cost will no longer be an issue.

(Continued)

The sequential treatment has been remarkable, with little toxicity other than the typical rash. It's unusual for the peripheral neuropathy associated with BV to be more intense than Grade 1, and in my experience it is usually reversible. Also, BV is associated with PML, which has been observed with almost all antibody-based treatments. I am not convinced that PML is causally related because the patients who develop PML have usually received a considerable amount of previous treatment. However, if patients experienced PML in the early-stage setting, that would pose a major problem for BV. Some recent evidence suggests that BV induces pancreatitis, a toxicity reported with other microtubule inhibitors.

In my practice I use BV according to its label. I administer BV to patients who are transplant ineligible and in cases of post-transplant failure.

Interview with Craig Moskowitz, MD, July 17, 2013

Phase 1/2 Study of Brentuximab Vedotin in Pediatric Patients with Relapsed or Refractory (R/R) Hodgkin Lymphoma (HL) or Systemic Anaplastic Large-Cell Lymphoma (sALCL): Preliminary Phase 2 Data for Brentuximab Vedotin 1.8 mg/kg in the HL Study Arm

Locatelli F et al.

Proc ASH 2013;Abstract 4378.

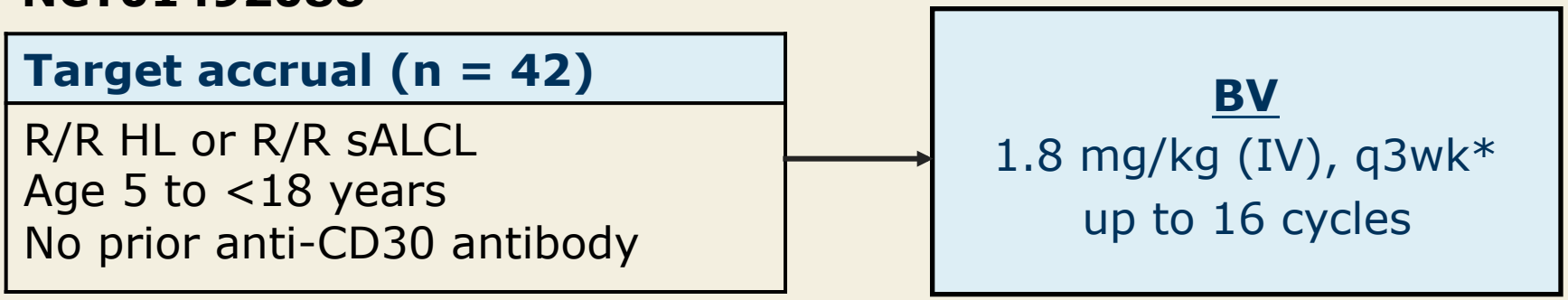
Background

- Brentuximab vedotin (BV) is an antibody-drug conjugate (ADC) containing an anti-CD30 monoclonal antibody.
- Pivotal Phase II studies have reported that BV is effective in Hodgkin lymphoma (HL) and sALCL with a manageable toxicity profile (*JCO* 2012;30:2183; *JCO* 2012;30:2190).
  - These studies led to its FDA approval for use in adult patients with relapsed or refractory (R/R) HL and R/R sALCL in 2011.
- Data from studies of BV in children with these lymphomas are currently limited but promising.
- **Study objective:** To report the preliminary efficacy, safety and pharmacokinetic (PK) findings from the Phase II study of BV in pediatric patients with R/R HL.

Locatelli F et al. *Proc ASH* 2013;Abstract 4378.

Ongoing Phase I/II Trial Design

NCT01492088



* The Phase I portion established the recommended Phase II dose (RP2D) as 1.8 mg/kg every 3 weeks

- **Phase II primary endpoint:** Overall response rate (ORR) at RP2D
- **Phase II secondary endpoints include:** Overall and progression-free survival, PK characterization, safety and determination of immunogenicity of BV

Locatelli F et al. *Proc ASH* 2013;Abstract 4378.

Patient Characteristics

Patients with R/R HL	n = 16
Median relative dose intensity	100%
Median age (range)	15 years (8-18)
Male	56%
Ann Arbor stage at initial diagnosis Stage I Stage II Stage III Stage IV Not specified	 0% 44% 6% 44% 6%
With B symptoms at baseline	50%

- The median dose of BV received was 435.5 mg (range, 128-2,036)

Locatelli F et al. *Proc ASH* 2013;Abstract 4378.

Response in Patients with R/R HL

Best response	n = 15*
ORR	47%
Complete response	33%
Partial response	13%

* Patients with available data at cutoff

- Responses were evaluated after 2 cycles of therapy
- The median duration of treatment was 114.5 days (range, 41-357)

Locatelli F et al. *Proc ASH* 2013;Abstract 4378.

Secondary Endpoints: Patients with R/R HL

Clinical outcome	
Median time to progression (n = 15)	4.8 months
Median time to response (n = 15)	2.7 months
Median duration of response (n = 7)	Not estimable
Median event-free survival (n = 16)	2.1 months
Median progression-free survival (n = 16)	2.8 months

Locatelli F et al. *Proc ASH* 2013;Abstract 4378.

Study Outcomes in R/R HL

- At data cutoff (October 8, 2013), patients (n = 16) had received a median of 4.5 cycles of BV.
- Patients discontinued treatment (n = 14):
  - Due to progressive disease (n = 8)
  - Due to adverse events (AEs) (n = 3)
  - Due to hematopoietic stem cell transplant (n = 1)
  - Due to unspecified reasons (n = 2)

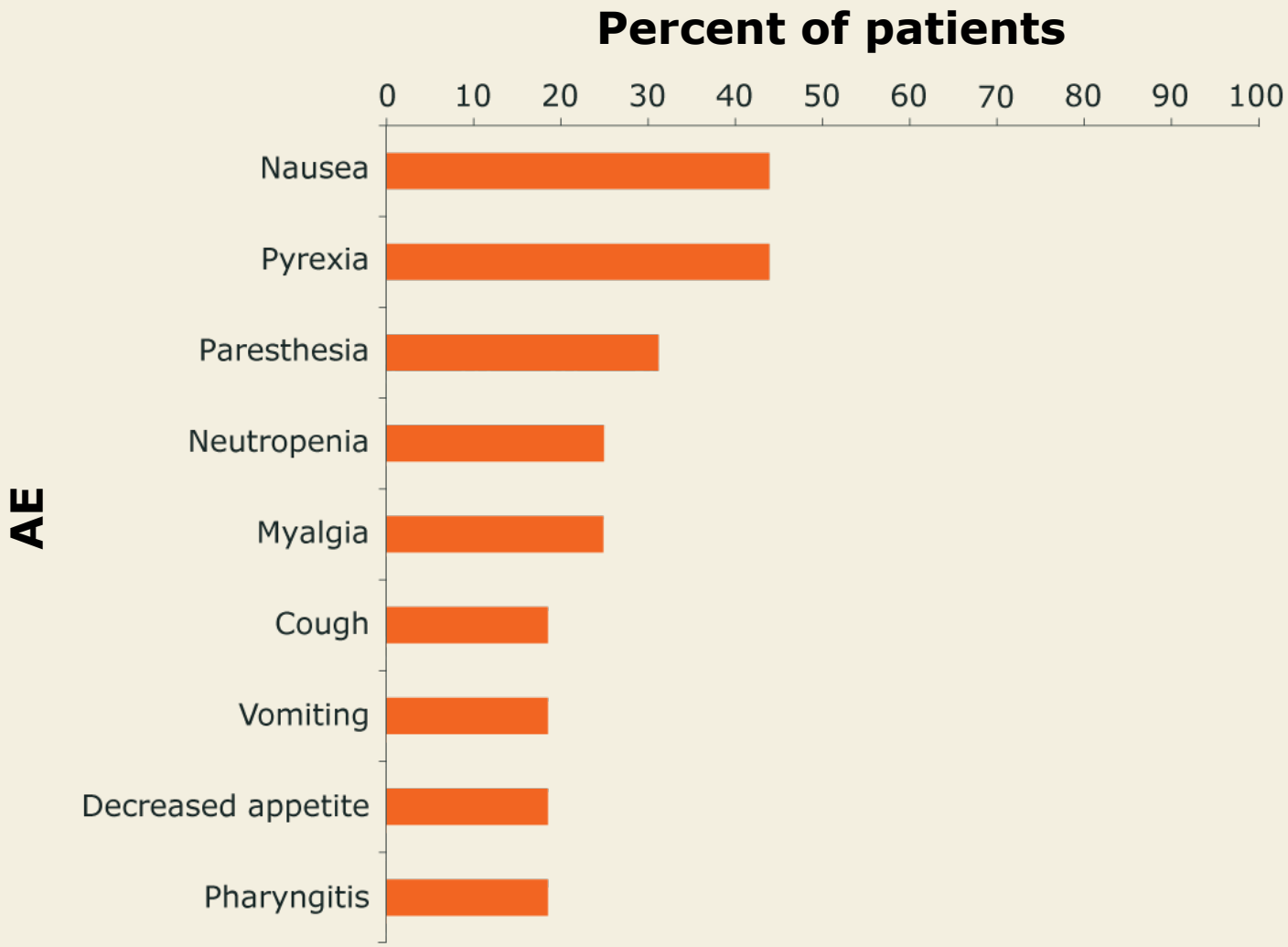
Locatelli F et al. *Proc ASH* 2013;Abstract 4378.

PK Analysis (R/R HL)

- Serum concentrations of BV, the microtubule-disrupting monomethyl auristatin E (MMAE) component of BV and total therapeutic antibody were determined.
- PK analysis demonstrated that:
  - Serum BV and therapeutic antibody concentrations peaked just after infusion.
  - The plasma MMAE concentration peaked 2 days after each infusion of BV, as expected with ADCs.
  - Over the treatment period, BV was detectable in blood prior to the next infusion.
    - Thus, patients remain exposed to BV from cycle to cycle.

Locatelli F et al. *Proc ASH* 2013;Abstract 4378.

Most Common AEs of All Grades (≥3 Patients with R/R HL)



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Serious AEs (SAEs) in R/R HL

SAEs	Patient ID	Intensity	Cycle, day
Hepatotoxicity*† Febrile neutropenia*	1	Grade 3 Grade 3	C1, D13 C1, D14
Supraventricular tachycardia	2	Grade 2	C2, D2
Cardiac arrest†	3	Grade 5	C2, D4
Pneumonia*	4	Grade 3	C2, D12
Pyrexia Pyrexia Vomiting	5	Grade 3 Grade 2 Grade 1	C2, D20 C3, D3 C3, D3
Anaphylactic reaction*	6	Grade 3	C6, D1

* BV-related SAE

† SAE resulting in BV discontinuation

Locatelli F et al. *Proc ASH* 2013;Abstract 4378.

Author Conclusions

- For the majority of the pediatric patients with R/R HL, treatment-emergent AEs ranged from mild to moderate.
- The most common treatment-emergent AEs (≥5/16 patients) were nausea, pyrexia and paresthesia.
- Four Grade ≥3 SAEs considered to be treatment-related events were observed (n = 3):
  - Hepatotoxicity (n = 1)
  - Febrile neutropenia (n = 1)
  - Pneumonia (n = 1)
  - Anaphylactic reaction (n = 1)

Locatelli F et al. *Proc ASH* 2013;Abstract 4378.

Author Conclusions (Continued)

- Three patients discontinued treatment due to AEs:
  - Hepatotoxicity (Grade 3)
  - Peripheral neuropathy (Grade 3)
  - Cardiac arrest (Grade 5)
- BV was detectable in the blood just prior to the next infusion. Therefore, patients remained exposed to treatment from cycle to cycle.
- BV demonstrated activity in this patient population.
  - Complete response: 33%
  - Partial response: 13%
- The Phase II part of the study is ongoing to determine the ORR with BV in 15 response-evaluable pediatric patients with R/R sALCL, including ≥10 patients in first relapse.

Locatelli F et al. *Proc ASH* 2013;Abstract 4378.

Investigator Commentary: Phase I/II Study of BV in Pediatric Patients with R/R HL or sALCL: Preliminary Phase II Data for BV in HL

HL in pediatric patients exists along the continuum with young adults and adults. This is a logical extension of BV into this population of patients. In this trial, 16 patients with R/R HL with a median age of 15 years were enrolled. About half of the patients were male and half were female, as can be expected for HL in the pediatric population.

The ORR was 47% with a complete response rate of 33%, and 13% of the patients achieved a partial response. These results are quite meaningful.

Interview with Christopher Flowers, MD, MS, February 24, 2014

A Phase I Study of Panobinostat in Combination with ICE (Ifosfamide, Carboplatin and Etoposide) in Patients with Relapsed or Refractory Classical Hodgkin Lymphoma (cHL)

Oki Y et al.

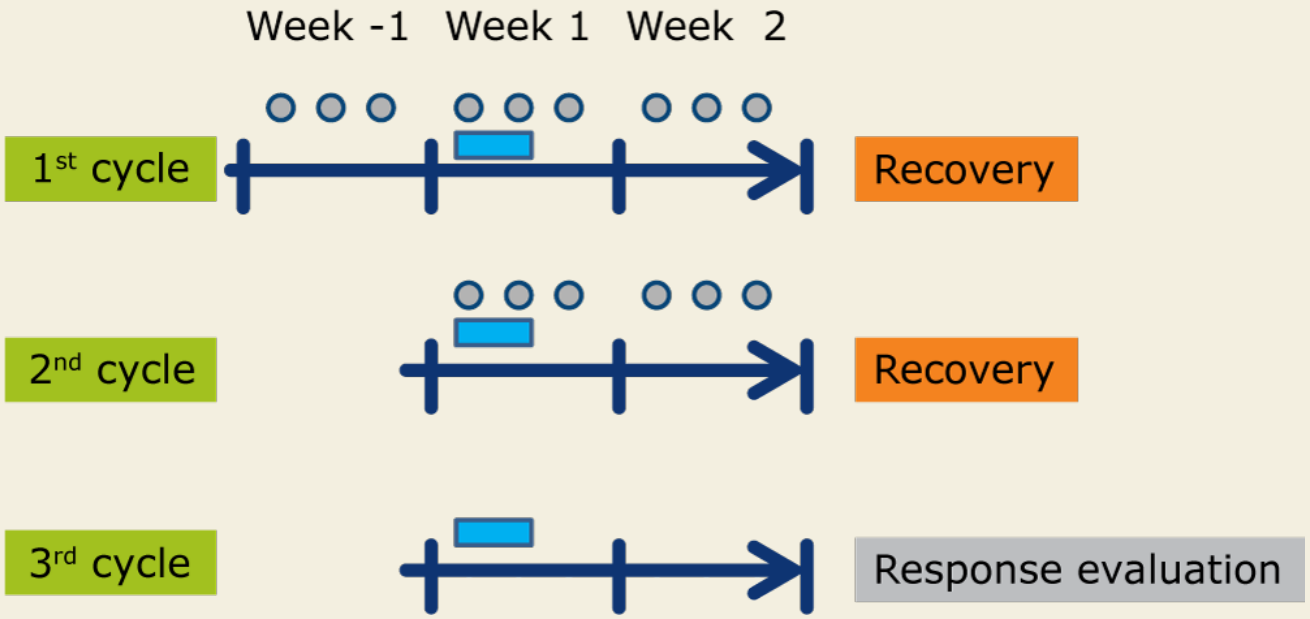
Proc ASH 2013;Abstract 252.

Background

- The standard approach for refractory or recurrent cHL is treatment with an effective salvage chemotherapy followed by stem cell transplantation.
- The commonly used regimen ICE produces complete response (CR) rates ranging from 26% (response evaluation by CT) to approximately 61% (with augmented ICE; response evaluation by PET) (*Blood* 2001;97:616; 2012;119:1665).
- Panobinostat, a potent oral pan-deacetylase inhibitor, has shown activity in relapsed/refractory cHL after transplant with an acceptable toxicity profile (*JCO* 2012;30:2197).
- **Study objective:** To evaluate the efficacy and safety of panobinostat in combination with ICE for relapsed/ refractory cHL.

Oki Y et al. *Proc ASH* 2013;Abstract 252.

Phase I Study Design — Schedule A

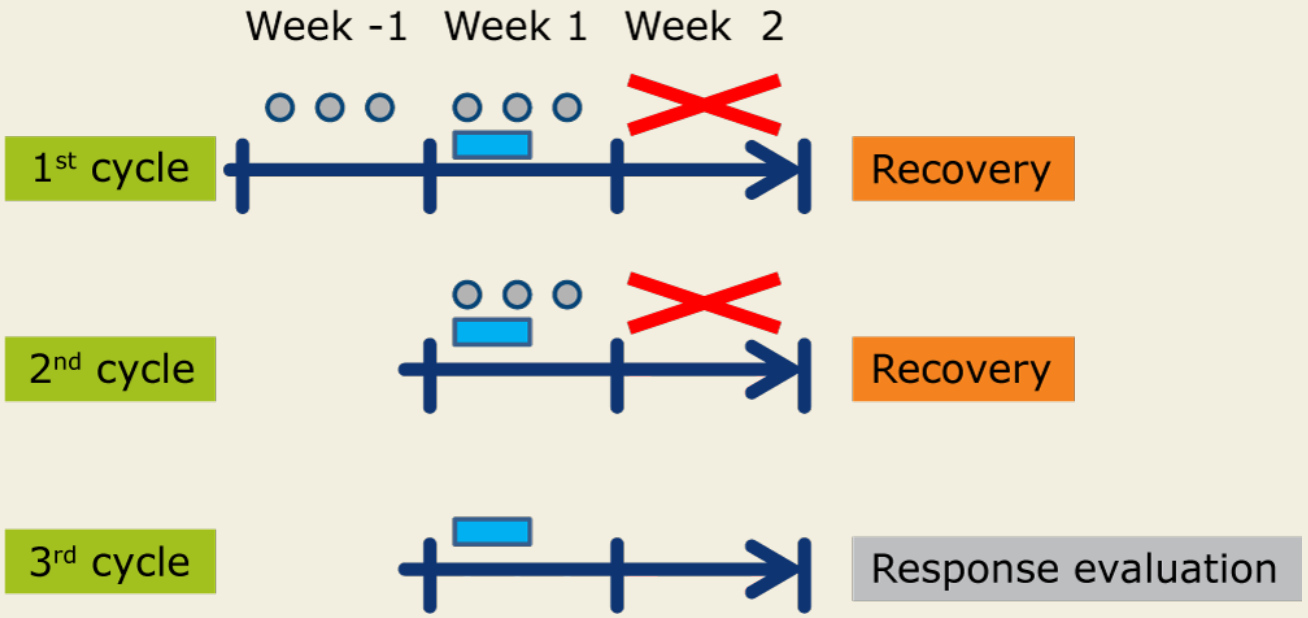


Panobinostat
Three times a week (M/W/F)
Start 1 week prior to ICE
Initial dose 20 mg po (M/W/F)
Escalate to 30 mg po (M/W/F)

ICE
Ifosfamide 5 g/m^2 on day 1
Carboplatin AUC 5 on day 1
Etoposide 100 mg/m^2 on days 1-3

Oki Y et al. *Proc ASH* 2013;Abstract 252.

Phase I Study Design — Schedule B



Panobinostat
Three times a week (M/W/F)
Start 1 week prior to ICE
30 mg po (M/W/F)

ICE
Ifosfamide 5 g/m^2 on day 1
Carboplatin AUC 5 on day 1
Etoposide 100 mg/m^2 on days 1-3

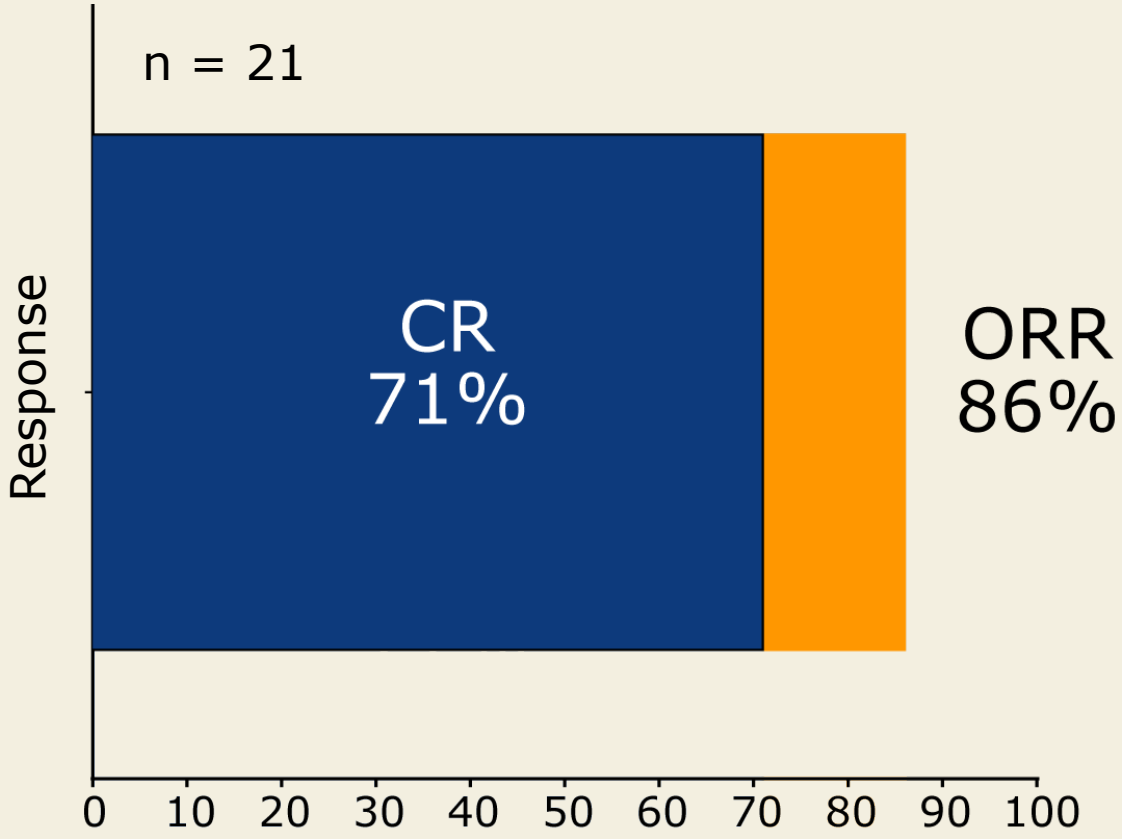
Oki Y et al. *Proc ASH* 2013;Abstract 252.

Eligibility and Cohorts

- **Eligibility:** Relapsed/refractory cHL after front-line anthracycline-containing regimen
- 21 patients evaluable (25 patients treated)
  - Primary refractory disease (n = 9)
- **Primary endpoint:** Determination of the recommended Phase II dose of panobinostat (maximum tolerated dose and different dosing schedules)
- **Secondary endpoints:** Toxicity, response rate
- **Cohort assignment**
  - Cohort 1 (schedule A): 20 mg, 12 doses (n = 6, dose-limiting toxicity [DLT] in 1)
  - Cohort 2 (schedule A): 30 mg, 12 doses (n = 3, no DLT)
  - Expansion cohort (schedule A): 30 mg, 12 doses (n = 10)
  - Expansion cohort (schedule B): 30 mg, 9 doses (n = 6, 4 patients under treatment not included in analysis)

Oki Y et al. *Proc ASH* 2013;Abstract 252.

Response



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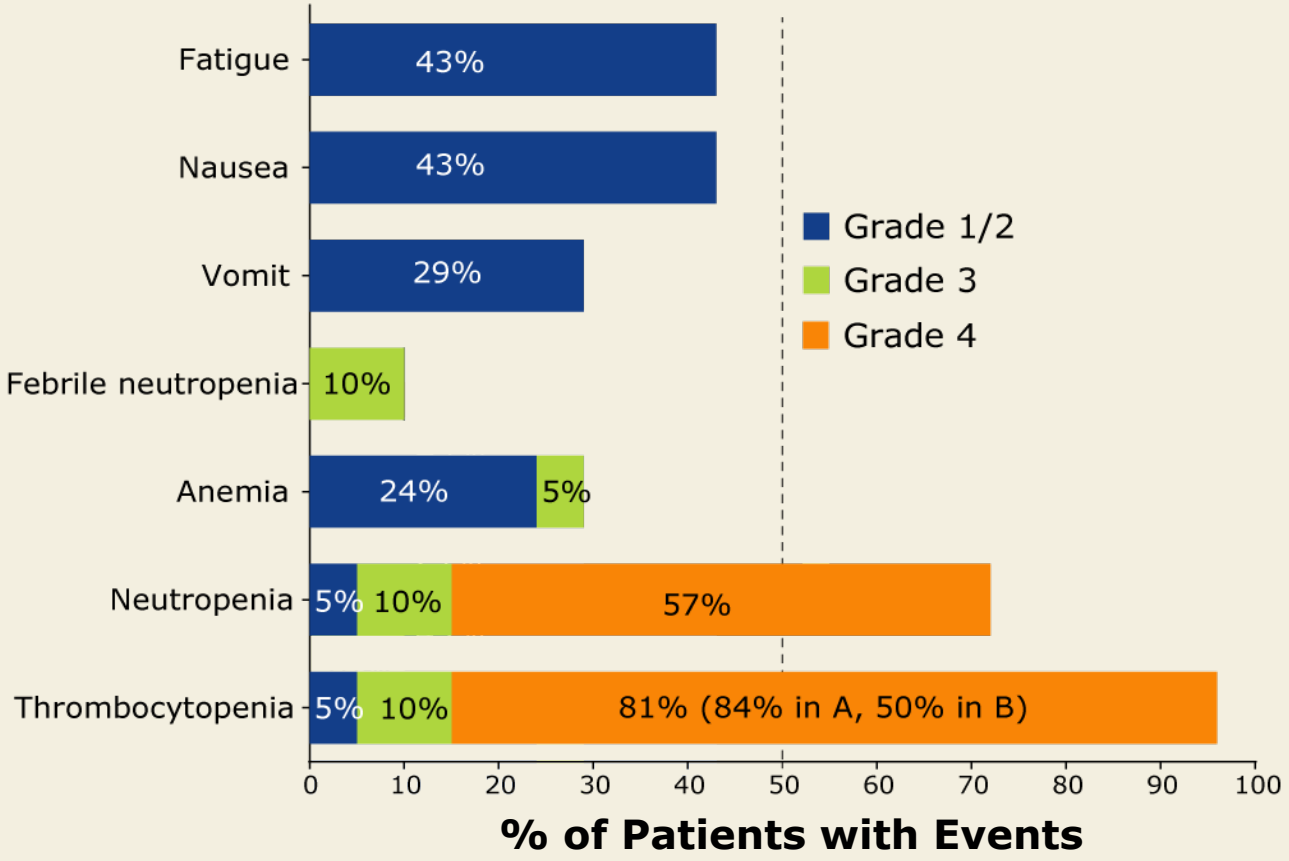
Subsequent Treatment

- 17 responding patients received autologous stem cell transplant without additional treatment except mobilization chemotherapy.
- 3 patients received one or more additional therapies followed by autologous stem cell transplant.
- All 20 patients had successful harvest and engraftment.

Oki Y et al. *Proc ASH* 2013;Abstract 252.

Adverse Events (N = 21)



- No Grade 3-4 nonhematologic toxicity
- Grade 4 thrombocytopenia: 84% (schedule A); 50% (schedule B)
- No deaths

With permission from Oki Y et al. *Proc ASH* 2013;Abstract 252.

Author Conclusions

- Panobinostat with ICE as a salvage treatment for cHL has acceptable toxicity and promising efficacy, with a CR rate of 71%.
- An alternative schedule (schedule B) is currently accruing patients.

Oki Y et al. *Proc ASH* 2013;Abstract 252.

Investigator Commentary: Phase I Study of Panobinostat with ICE in Relapsed/Refractory cHL

Panobinostat emerged around the same time as brentuximab vedotin as a promising agent for relapsed/refractory HL. Early evidence suggested activity of HDAC inhibitors, in particular panobinostat, in patients with HL. However, although brentuximab vedotin received FDA approval and is now incorporated into therapy for relapsed/refractory HL, panobinostat has not been approved.

This Phase I study employed a 3 + 3 design to identify the dose of panobinostat that could be used safely in combination with standard ICE chemotherapy as a salvage regimen for relapsed/refractory HL. With the combination, fatigue was a frequent side effect in 43% of patients, as reported in other studies with HDAC inhibitors.

(Continued)

Nausea and vomiting occurred in 43% and 29% of the patients, respectively. Some hematologic toxicities were also observed, as would be expected with the ICE regimen.

The overall response rate of 86% and complete response rate of 71% with panobinostat/ICE are higher than what might be anticipated with ICE therapy alone. However, further randomized studies comparing the combination to ICE alone as a salvage regimen are needed before definitive conclusions can be made.

Interview with Christopher Flowers, MD, MS, February 24, 2014

Gray Zone Lymphoma (GZL) with Features Intermediate between Classical Hodgkin Lymphoma (cHL) and Diffuse Large B-Cell Lymphoma (DLBCL): A Large Retrospective Multicenter Analysis of Clinical Characteristics, Treatment, Outcomes, and Prognosis in the Current Era

Evens AM et al.

Proc ASH 2013;Abstract 847.

Background

- GZL is recognized by the WHO as a category of B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and cHL.
- GZL is uncommon and is reported to present primarily with mediastinal involvement, with very few nonmediastinal presentations reported.
- Treatment of GZL is challenging due to disease heterogeneity, lack of data regarding prognostication and no standard guidelines for management (*Curr Hematol Malig Rep* 2012;7:241).
- **Study objective:** To conduct a large retrospective multicenter analysis of clinical characteristics, treatment, outcomes and prognosis of patients with GZL.

Evens AM et al. *Proc ASH* 2013;Abstract 847.

Study Design

- Multicenter retrospective analysis of patients with newly diagnosed GZL treated from 2003 to 2012 at 18 North American academic centers
- Inclusion criteria included availability of clinical information and a minimum follow-up of 12 months for nonrelapsing patients
- 96 patients analyzed (100 patients identified, 4 excluded for inadequate follow-up)
- Diagnosis established by institutional expert pathology review
- Patient characteristics, treatment and outcome were examined, and prognostic factors associated with survival on univariate and multivariate Cox regression analyses were determined

Evens AM et al. *Proc ASH* 2013;Abstract 847.

Clinical Characteristics at Diagnosis

Characteristic	(n = 96)
Median age (range)	39 y (19-86)
ECOG PS 0-1	89%
Male:female ratio	1.5:1
Stage III/IV	52%
Bulky disease (>10 cm)	23%
Mediastinal involvement	45%

- Other characteristics: Bone marrow involvement 13%, nonmarrow EN disease 48%, IPI 3-5: 23%, IPS 4-7: 13%

Evens AM et al. *Proc ASH* 2013;Abstract 847.

Mediastinal versus Nonmediastinal GZL

Characteristic	Mediastinal (n = 43)	Nonmediastinal (n = 53)	*p*-value
Age, years (range)	37 (19-72)	50 (20-86)	0.0001
Male-female ratio	1.3	1.9	0.09
Bulk (>10 cm)	42%	8%	<0.0001
>1 EN site*	11%	33%	0.02
Stage III/IV	14%	83%	<0.0001
IPI 3-5	5%	32%	0.0001
IPS 4-7	2%	21%	0.004

* Most common nonmarrow sites: Mediastinal — lung n = 8; Nonmediastinal — bone n = 10, lung n = 9, liver n = 4

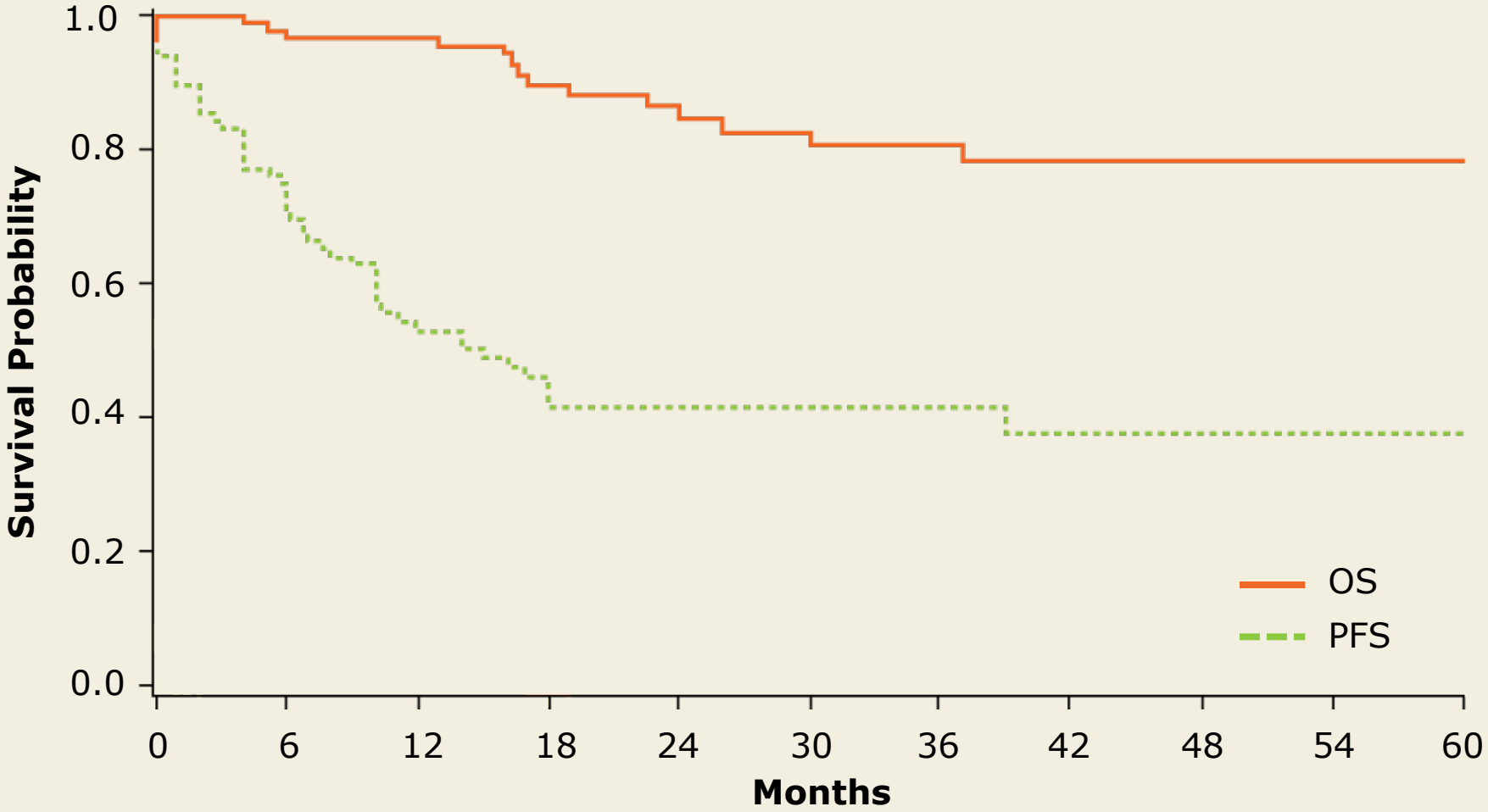
Evens AM et al. *Proc ASH* 2013;Abstract 847.

Treatment and Outcome

- First-line chemotherapy received: CHOP 58%, ABVD 26%, EPOCH 10%, BEACOPP or hyperCVAD 5%, other 1%
- Patients receiving rituximab as part of first-line therapy: 69%
- Patients receiving consolidative radiation therapy: 31%
- Overall response rate (ORR) to first-line therapy: 70% (58% complete remission [CR])
  - Mediastinal 67% (58% CR) versus nonmediastinal 71% (58% CR)
- ORR by front-line therapy: R-CHOP 71%, R-EPOCH 90%, ABVD 50%
- 2-year progression-free survival (PFS): Rituximab: yes 49% versus no 27%, $p = 0.10$
- 4-year PFS, Stage I/II: yes 52%, no 32%, $p = 0.02$
- 4-year overall survival (OS), Stage I/II: yes 97%, no 71%, $p = 0.003$

Evens AM et al. *Proc ASH* 2013;Abstract 847.

Survival: All Patients



2-year PFS 41%, OS 84% (median follow-up 25 months)

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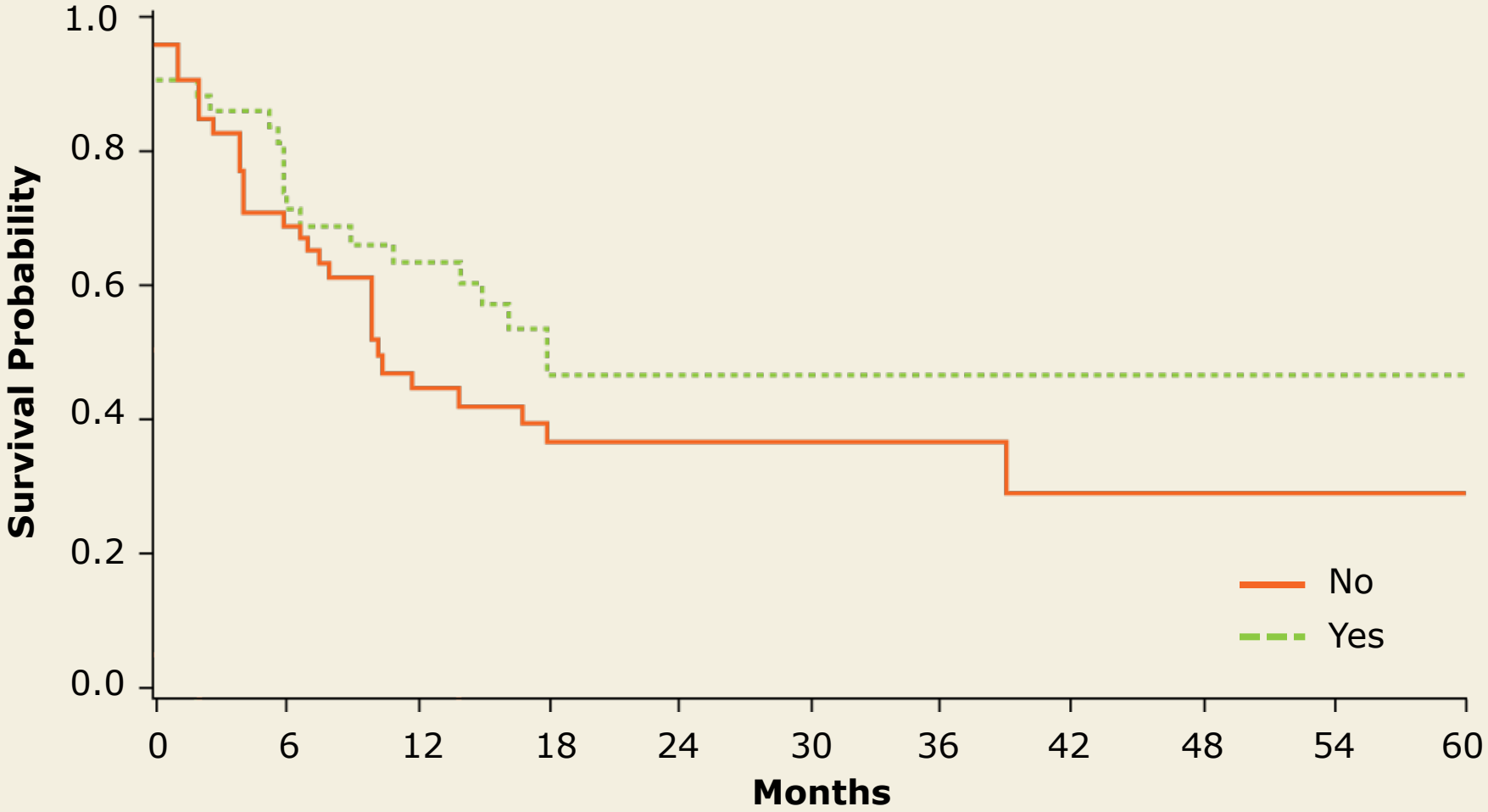
PFS Subset Analyses: Mediastinal versus Nonmediastinal



2-year PFS mediastinal: Yes 47% versus No 37%, $p = 0.27$

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Prognosis — Univariate Analysis

	PFS		OS	
Characteristics (at diagnosis)	**HR**	***p*-value**	**HR**	***p*-value**
Stage (III/IV vs I/II)	1.91	0.03	11.85	0.02
Stage (IV vs I-III)	2.76	0.0004	7.05	0.004
Prognostic scores	**HR**	***p*-value**	**HR**	***p*-value**
IPI (3-5 vs 0-2) IPS (3-7 vs 0-2)	2.50 1.91	0.006 0.06	3.89 4.77	0.03 0.06

- Other prognostic factors evaluated for PFS: performance status (2-4 vs 0-1), HR 3.44, $p = 0.001$; hemoglobin <10.5 g/dL, HR 2.13, $p = 0.02$; elevated LDH, HR 2.03, $p = 0.025$
- Other prognostic factors evaluated for OS: hypoalbuminemia, HR 3.14, $p = 0.08$; B symptoms (yes vs no), HR 7.8, $p = 0.05$

Evens AM et al. *Proc ASH* 2013;Abstract 847.

Prognosis — Multivariate Analysis

- On multivariate regression analysis for PFS, elevated LDH predicted poorer outcome (HR 2.01, $p = 0.05$).
- Factors significant for inferior OS:
  - Presence of B symptoms (HR 17.41, $p = 0.02$)
  - Hypoalbuminemia (HR 8.09, $p = 0.02$)
  - Stage IV versus I-III disease (HR 21.39, $p = 0.003$)

Evens AM et al. *Proc ASH* 2013;Abstract 847.

Author Conclusions

- GZL is an important entity to recognize.
- Nonmediastinal GZL has distinct characteristics (age, bulk, EN, stage).
- PFS (all patients) appeared inferior to that expected in cHL and DLBCL, though OS was good.
- B symptoms, albumin and stage are critical prognostic factors for OS.
- Continued analysis is warranted (eg, pathology and salvage therapy).

Evens AM et al. *Proc ASH* 2013;Abstract 847.

Investigator Commentary: GZL with Features between cHL and DLBCL — Retrospective Analysis

This study was conducted to understand the characteristics, treatment, outcomes and prognosis of patients with GZL, which is a challenging subset of lymphomas to manage. GZL are B-cell lymphomas that are not clearly classifiable as one subtype or another. They are commonly thought to have features intermediate between HL and primary mediastinal DLBCL and typically present in the mediastinum.

A key feature of this study was that a new group of GZL was identified that did not have mediastinal involvement, which was about half of the patients with GZL. A wide array of first-line chemotherapy regimens were administered to these patients. A trend toward a benefit for rituximab was seen, but a fair amount of heterogeneity among the patient characteristics and the types of regimens was also present. Hence, it's difficult to conclude that one approach was superior to the others. The 2-year PFS of 41% and OS of 84% suggest that the outcome can be quite varied and may differ from that with both DLBCL and HL. This is a patient population for whom we need to conduct additional studies and identify specific therapies.

Interview with Christopher Flowers, MD, MS, February 24, 2014

Reduced-Intensity Conditioning (RIC) and Allogeneic Stem Cell Transplantation (allo-SCT) for Relapsed/Refractory Hodgkin Lymphoma (HL) in the Brentuximab Vedotin Era: Favorable Overall and Progression-Free Survival (OS/PFS) with Low Transplant-Related Mortality (TRM)

Anderlini P et al.

Proc ASH 2013;Abstract 410.

Background

- In Hodgkin lymphoma (HL), progressive disease (PD) remains the main cause of treatment failure after reduced-intensity conditioning (RIC) allogeneic stem cell transplantation (allo-SCT).
- Fludarabine (F) and melphalan (M) (FM) as a preparative regimen for RIC allo-SCT in relapsed or refractory (R/R) HL is associated with improved patient outcomes (*Haematologica* 2008;93:257).
- In August 2007, gemcitabine (G), a highly active agent, was added to FM as a RIC regimen for allo-SCT in R/R HL, and the main nonhematologic toxicities were pulmonary, skin related and mucositis (*Leuk Lymphoma* 2012;53:499).
- Subsequently, brentuximab vedotin (BV) was introduced as salvage therapy prior to allo-SCT to maximize response.
- **Study objective:** To augment cytoreduction before transplant and improve overall survival (OS) and progression-free survival (PFS) while reducing PD in R/R HL.

Anderlini P et al. *Proc ASH* 2013;Abstract 410.

Study Methods

- Between August 2007 and April 2013, patients with HL who underwent allo-SCT with the G-FM regimen (n = 27)
- Patients who received BV prior to allo-SCT (n = 14)
  - Patients for whom BV was the last therapy prior to allo-SCT (n = 7)
- Patients for whom the donor was an HLA-identical sibling (n = 16)
- Patients for whom the donor was a matched unrelated donor (MUD) (n = 11)

Anderlini P et al. *Proc ASH* 2013;Abstract 410 (abstract only).

Study Methods (Continued)

- The conditioning regimen:
  - G: 800 mg/m^2 (IV) x 1
  - F: 33 mg/m^2 (IV) daily x 4
  - M: 70 mg/m^2 (IV) daily x 2
- For patients with a MUD, thymoglobulin (4 mg/kg, IV) was added
- Patients who received peripheral blood progenitor cells (n = 20)
- Patients who received bone marrow transplant (n = 7)

Anderlini P et al. *Proc ASH* 2013;Abstract 410 (abstract only).

Patient Characteristics

- All patients had experienced PD on multiple conventional treatments (n = 27)
  - Median age of patients: 31 years (range, 20-46)
  - Median number of prior chemotherapy regimens: 4
  - Radiation therapy: 44%
  - Prior autologous (auto) SCT: 70%
- Disease status at SCT was:
  - CR or undetermined CR (CRu): 63%
  - Partial response: 33%
  - Other: 4%
- Median time to PD after auto-SCT: 5 months (range, 1-68)

Anderlini P et al. *Proc ASH* 2013;Abstract 410 (abstract only).

Study Outcomes

- Myeloid recovery was prompt with an absolute neutrophil count of >500/mcL at day 11+ (median)
- Median platelet recovery at 20K/mcL was at day 13+
- In 23 evaluable patients, chimerism studies indicate 100% donor-derived engraftment
- Early deaths (before day 30): n = 3
- Number of cases of graft failure: n = 1
- Cumulative incidence of:
  - Day 100 transplant-related mortality (TRM): 15%
  - Overall TRM: 15%
- Cumulative incidence of acute (Grade 2-4) and chronic graft versus host disease (extensive): 19% versus 39%, respectively

Anderlini P et al. *Proc ASH* 2013;Abstract 410 (abstract only).

Responses

Overall response rate (CR/CRu)	BV treated (n = 14)	BV naïve (n = 13)	*p*-value
Prior to allo-SCT	79%	46%	0.12
After allo-SCT	85%	85%	NSD

NSD = no significant difference

- All 7 patients who received BV as last line of therapy prior to allo-SCT achieved CR/CRu

Anderlini P et al. *Proc ASH* 2013;Abstract 410 (abstract only).

Survival Outcomes at Last Follow-Up

All patients	n = 27	95% CI
OS	69%	41-86
PFS	55%	31-74
Cumulative overall PD incidence	30%	15-61

- Deaths (n = 6)
  - Graft rejection (n = 1); pneumonia (n = 2); respiratory failure (n = 1); PD (n = 2)
- After a median follow-up of 18 months (range, 4-55)
  - Patients alive (n = 21)
- All 7 patients who received BV as last line of therapy prior to allo-SCT are alive

Anderlini P et al. *Proc ASH* 2013;Abstract 410 (abstract only).

FM versus G-FM as a RIC Regimen for Allo-SCT in R/R HL

Variable	FM140 (n = 58)	G-FM140 (n = 27)
Age (range)	32 years (19-59)	31 years (20-46)
Received BV before allo-SCT	0%	52%
Achieved CR/CRu before transplant	24%*	63%
TRM (day 100/overall)	7%/15%	15%/15%
2-year OS	64%	78%
2-year PFS	32%	55%
2-year PD	55%	30%
Median time to PD after allo-SCT	4.5 months	13 months

* Included 28 patients with <PR before transplant

- Cumulative proportion of patients with CR/CRu surviving and progression free at 18 months:
  - FM140 (57%) versus G-FM140 +/- BV (80%); $p = 0.2$

Anderlini P et al. *Proc ASH* 2013;Abstract 410 (abstract only).

Adverse Events (AEs) (N = 27)

AE	n (%)
All-grade pulmonary toxicity	9 (33%)
Grade 1-3	6 (22%)
Grade 4-5	3 (11%)
All-grade cutaneous toxicity*	5 (19%)
Grade 1-2	4 (15%)
Grade 3	1 (4%)
All-grade mucositis	13 (48%)
Grade 1-2	12 (44%)
Grade 3	1 (4%)

* Skin rash, responsive to steroidal therapy

Anderlini P et al. *Proc ASH* 2013;Abstract 410 (abstract only).

Author Conclusions

- The G-FM140 regimen continues to show promise in this group of patients with high-risk HL.
- The inclusion of G may affect pulmonary toxicity, but TRM remained low.
- With the current BV-supported approach, the CR rate before transplant may be improved.
  - 18-month PFS in patients who achieved CR/CRu before transplant seems to compare favorably to the FM140 experience in complete responders.
    - 80% versus 57%, $p = 0.20$
- Although this BV-based transplant strategy needs further evaluation, the role of RIC allo-SCT in HL may need to be reassessed in the BV era.

Anderlini P et al. *Proc ASH* 2013;Abstract 410 (abstract only).

Investigator Commentary: RIC and Allo-SCT for Patients with R/R HL in the Era of BV

RIC and allo-SCT is an approach that is used in the treatment of lymphomas probably because of the evidence of graft versus lymphoma effect and is a way of eradicating the disease. Although it is an approach that appears to be extraordinarily promising in mantle-cell lymphoma, chronic lymphocytic leukemia and follicular lymphoma, it seems to be less beneficial in HL. The challenge is to try to mitigate the toxicities and maximize the benefit of allo-SCT.

This study involved the use of allo-SCT with a RIC regimen including G-FM in 27 patients with R/R HL. The investigators looked specifically at patients who had received prior BV to see how their responses compared to other patients who underwent allo-SCT. Out of the 27 patients, 14 had received prior BV. All 7 patients who received BV as their last therapy achieved CR/CRu.

(Continued)

This is intriguing evidence that we may have a way of using BV prior to allo-SCT to maximize its efficacy. These data are provocative, but the effectiveness of this approach needs to be confirmed in other studies. These results may help to rejuvenate the use of allo-SCT for HL, for which the graft versus lymphoma benefit does not appear to be quite as great. Perhaps BV will help to extend that benefit.

Interview with Christopher Flowers, MD, MS, February 24, 2014