ADCETRIS™
Brentuximab Vedotin

CD30-Directed Therapy for Hodgkin Lymphoma

Oncologic Drugs Advisory Committee

July 14, 2011

SeattleGenetics®

Brentuximab Vedotin Hodgkin Lymphoma

Introduction

Elaine Waller, PharmD

Senior Vice President of Regulatory Affairs
Seattle Genetics

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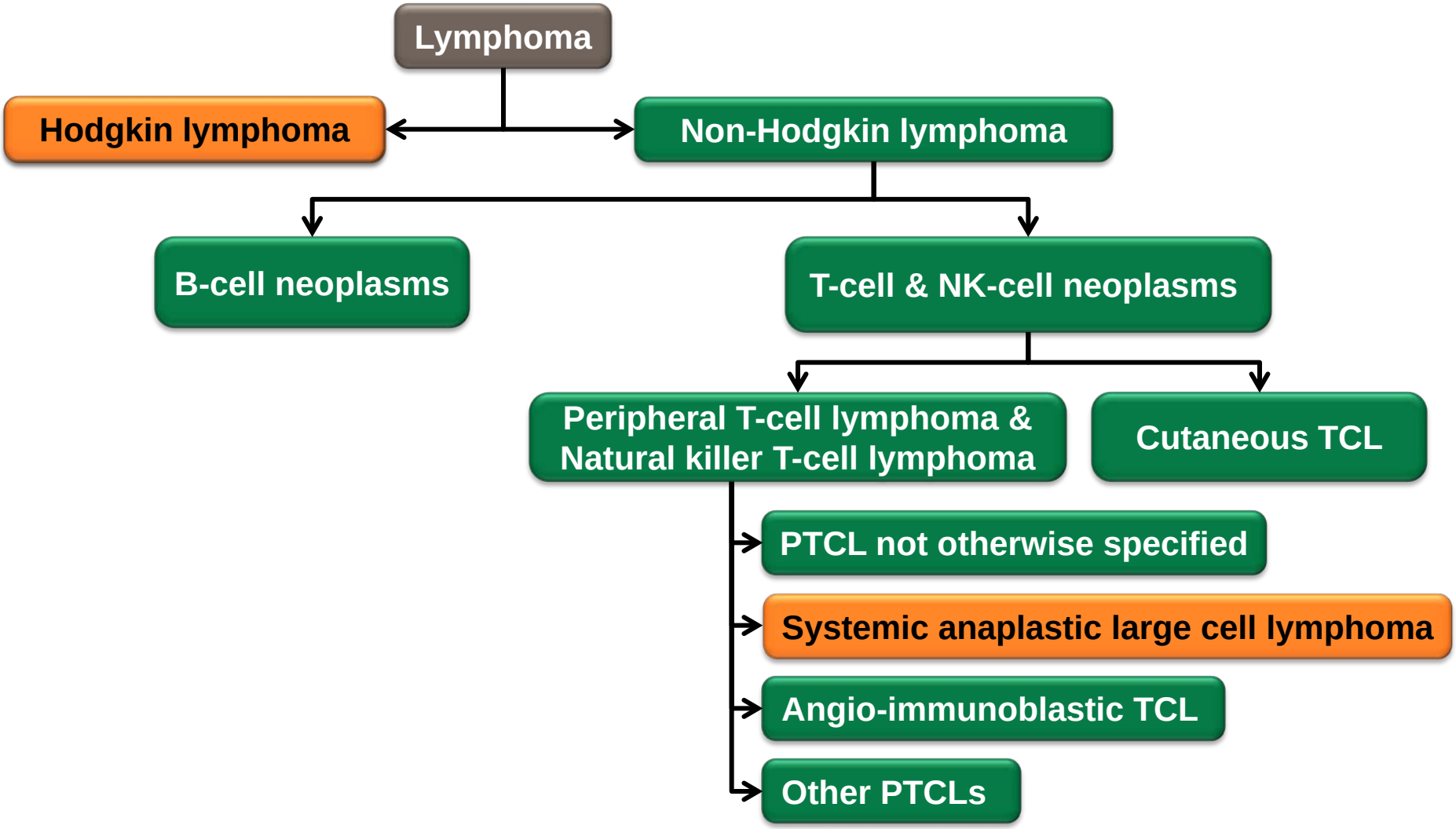
Brentuximab Vedotin Targets CD30 Antigen

- Transmembrane glycoprotein receptor, member of TNF receptor superfamily
- Leads to transduction of biologic signals, including cell proliferation
- Highly expressed on HL and ALCL cells
- Restricted distribution on normal cells:
  - Expressed on activated lymphocytes (B cell, T cell, NK cell)
  - Weakly expressed on activated monocytes

CD30+ Lymphomas



Comparison of Unconjugated CD30 mAb With Brentuximab Vedotin

Hodgkin Lymphoma

	CD30 mAb (unconjugated cAC10)	Brentuximab vedotin (conjugated cAC10)
Dose	6 or 12 mg/kg weekly	1.8 mg/kg every 3 weeks
Patients, n	38	102
Objective response rate	—	75%
Complete remissions	—	34%

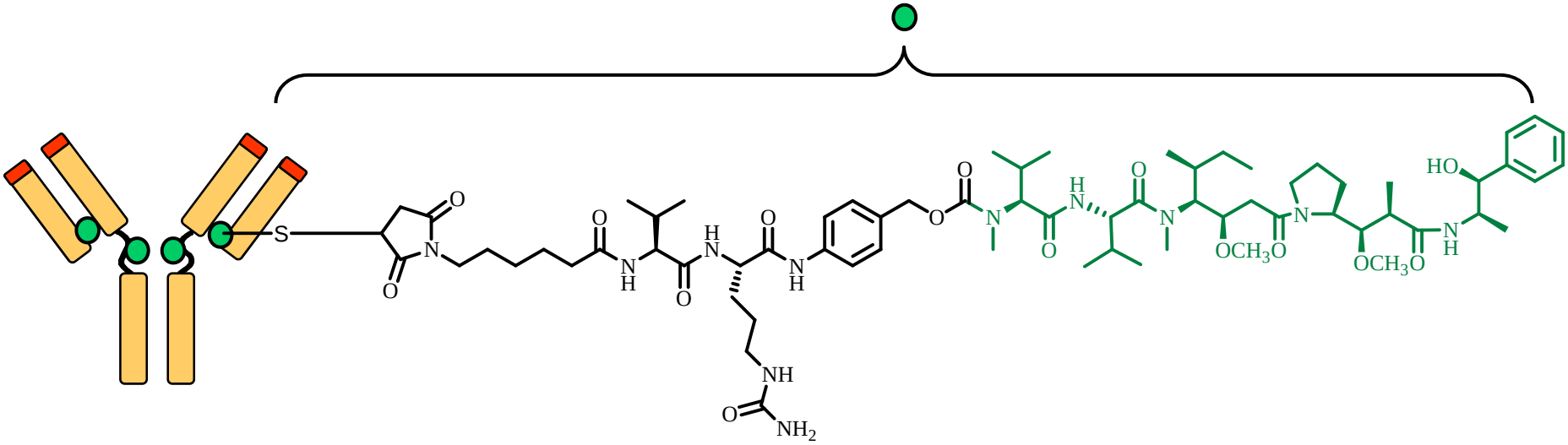
Forero-Torres A, et al. *Br J Haematol.* 2009;146:171-179.

Brentuximab Vedotin Structure

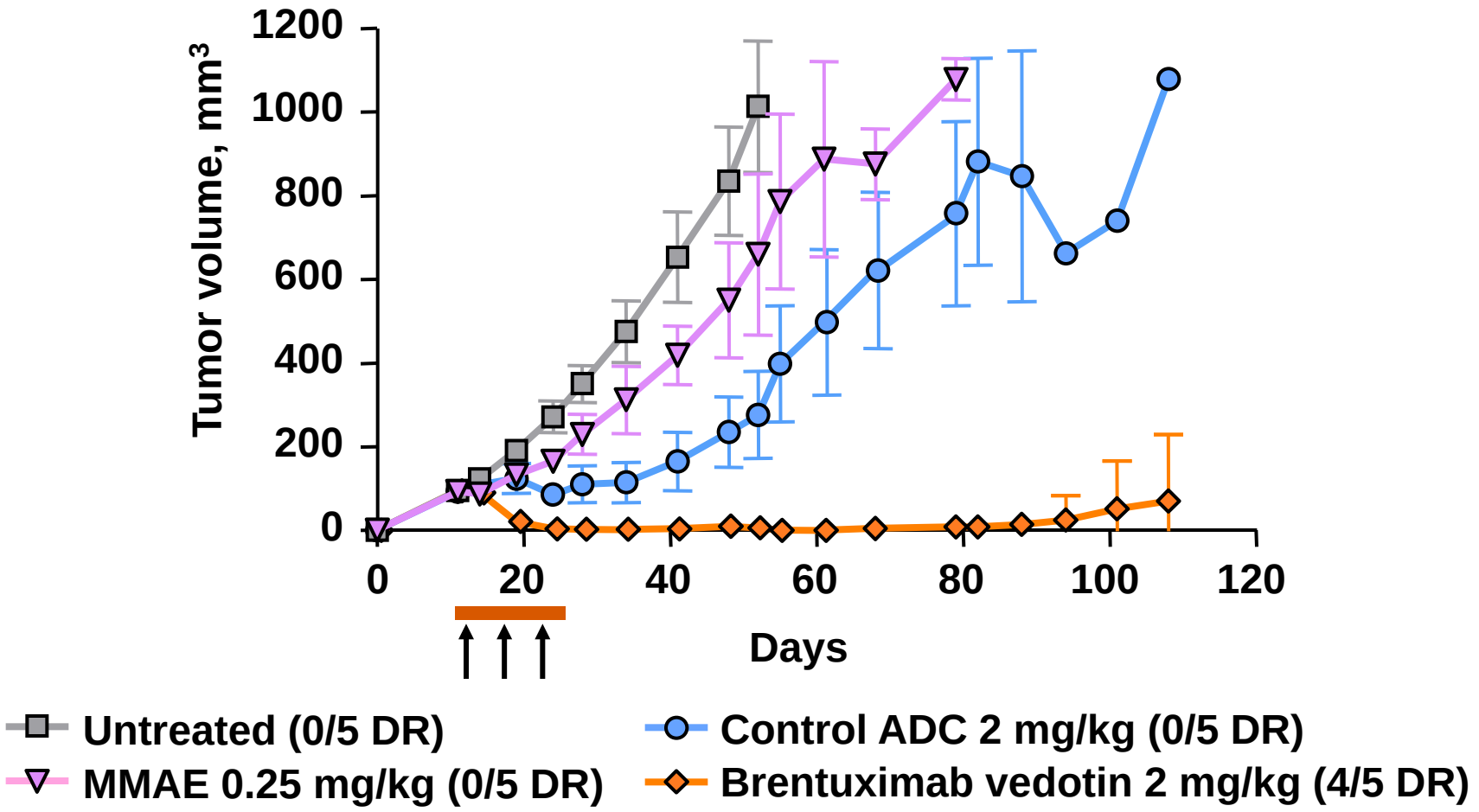
Antibody
cAC10 anti-CD30 antibody

Linker
Attachment group
Protease-cleavage site

Drug
MMAE
cytotoxic agent

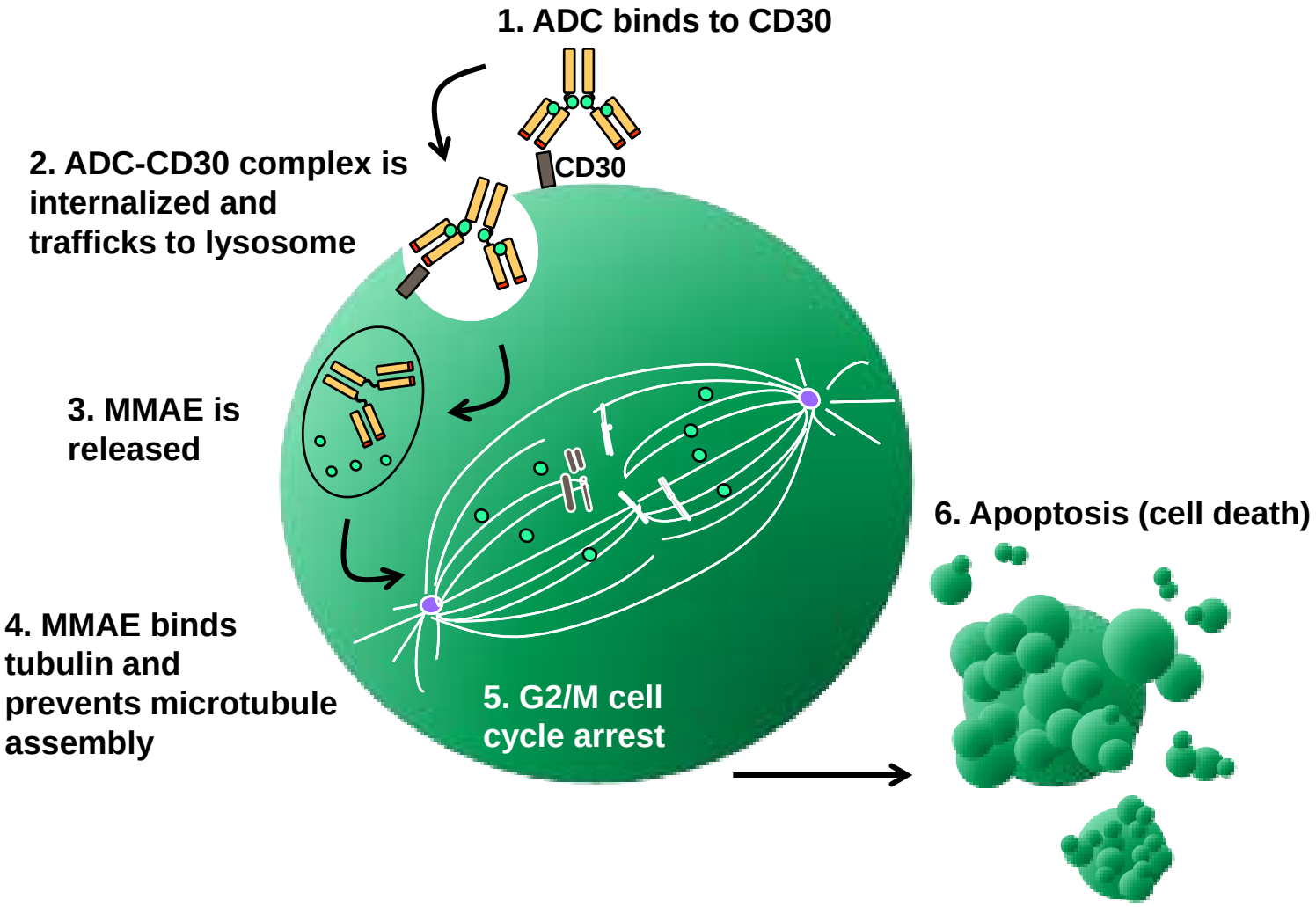


Brentuximab Vedotin Is More Active Than MMAE Alone



DR = Durable response.
HL L428 subcutaneous xenograft model in NSG mice (n = 5 group), mean ± SD, q4dx3.

Brentuximab Vedotin Mechanism of Action



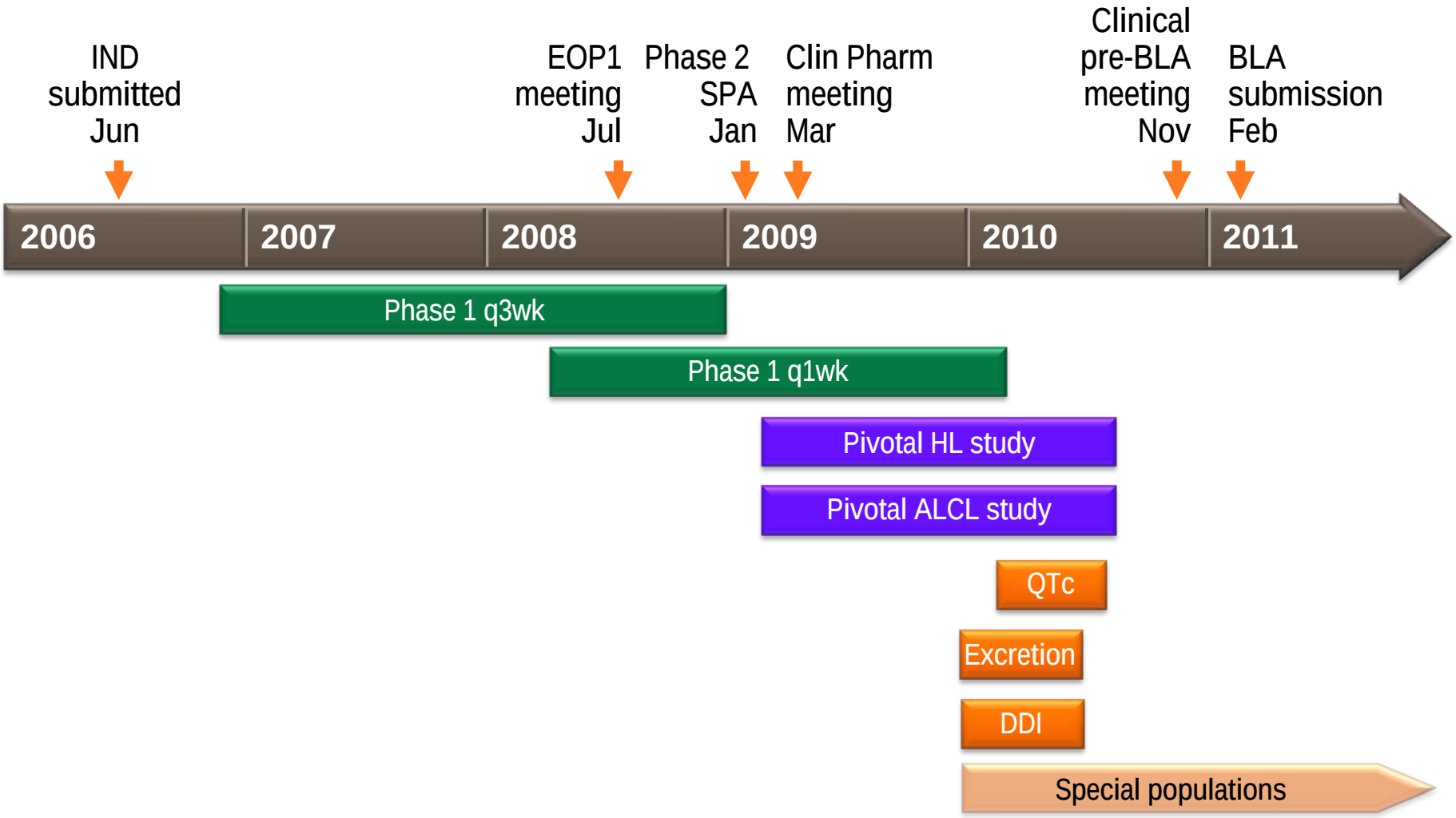
Proposed Indication and Dosage Regimen

- Brentuximab vedotin is a CD30-directed antibody-drug conjugate indicated for the treatment of patients with relapsed or refractory Hodgkin lymphoma
- Brentuximab vedotin 1.8 mg/kg administered as an IV infusion over 30 minutes every 3 weeks
- Treat until disease progression or unacceptable toxicity

Brentuximab Vedotin in Patients With Hodgkin Lymphoma

- Efficacy
  - Clinically relevant objective response rates
  - Durable complete remissions
  - Resolution of disease-related signs and symptoms
- Safety
  - Most common AEs were grade 1 and 2
  - Peripheral neuropathy is manageable

Clinical Trials Submitted in BLA



Special Protocol Assessment

- Agreements made with the FDA
  - Primary endpoint
    - ORR per independent review facility (IRF)
    - 2007 Revised Response Criteria for Malignant Lymphoma
  - ORR of 30% considered a meaningful response
  - Supporting evidence
    - Duration of response
    - Complete remission
    - B symptom resolution
    - Investigator assessment vs IRF concordance
- SPA remains in effect

AETHERA: Phase 3 HL Post-ASCT

- Randomized, double-blind, placebo-controlled, multicenter, phase 3 clinical trial
- Patients randomized 1:1 to receive brentuximab vedotin or placebo every three weeks
- Efficacy endpoints
  - Primary: Progression-free survival per IRF
  - Key Secondary: Overall survival
- Population (N = 322) includes at least one of the following
  - Refractory to front-line therapy
  - Relapsed within 12 months
  - Extranodal disease
- Stratified by response to frontline and salvage treatments

Ongoing Clinical Development in Hodgkin Lymphoma

- **AETHERA - Phase 3 trial in patients at high risk of residual HL following autologous SCT**
- **Phase 1 trial in front-line HL**
- **Expanded access program in relapsed or refractory HL and systemic ALCL**

Today's Agenda

Introduction	**Elaine Waller, PharmD** **Seattle Genetics**
CD30-Directed Therapy for Hodgkin Lymphoma	**Joseph M. Connors, MD, FRCPC** **British Columbia Cancer Agency**
Brentuximab Vedotin Hodgkin Lymphoma Efficacy Profile	**Eric Sievers, MD** **Seattle Genetics**
Brentuximab Vedotin Safety Profile	**Tom Reynolds, MD, PhD** **Seattle Genetics**
Hodgkin Lymphoma Benefit:Risk Profile	**Joseph M. Connors, MD, FRCPC** **British Columbia Cancer Agency**

Consultants

- David R. Cornblath, MD
  Professor, Neurology
  Johns Hopkins University
- L. Jeffrey Medeiros, MD
  Professor, Chair, Dept of Hematopathology
  MD Anderson Cancer Center
- Owen O'Connor, MD
  Deputy Director of Clinical Research and
  Cancer Treatment
  New York University Cancer Institute
- J. Michael O'Neal, MD
  Chief Medical Officer
  CoreLab Partners
- Barbara Pro, MD
  Associate Professor
  Fox Chase Cancer Center

Brentuximab Vedotin
CD30 Directed Therapy for Hodgkin Lymphoma

Joseph M. Connors, MD, FRCPC

Clinical Director, Centre for Lymphoid Cancer
British Columbia Cancer Agency
University of British Columbia

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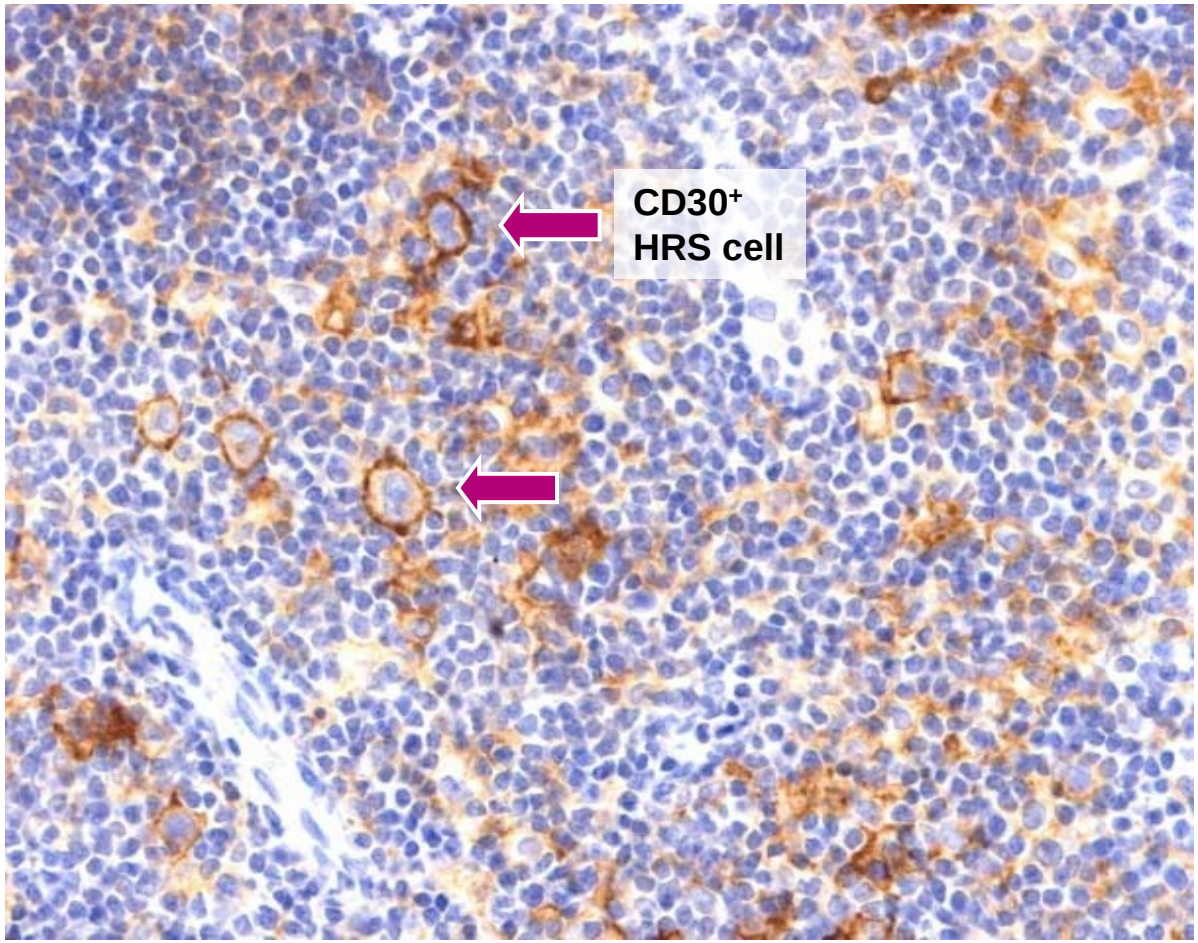
Disclosures

	Not-for-profit Sources	For-profit Sources
Institutional research support including clinical trials	Canadian Cancer Society Research Institute NCI of Canada Clinical Trials Group Terry Fox Foundation SWOG	Amgen Cephalon Genentech Hoffmann-La Roche Johnson & Johnson Bayer Healthcare Lilly Merck Roche Canada Seattle Genetics
Advisory Board/Committee	ASH ASCO Lymphoma Foundation Canada Lymphoma Research Foundation (US) NCIC Canada	None
Employee	British Columbia Cancer Agency	None
Speakers' Bureau	ASH	None
Honoraria	ASH, ASCO	None
Board member	None	None
Paid consultant	None	None
Stockholder	None	None

CD30: Optimal Target for Antibody-Drug Conjugate Therapy

- Highly restricted normal cell surface expression
- Defining marker for Hodgkin lymphoma—malignant Hodgkin Reed-Sternberg cells
- Standard immunohistochemical test
  - Widely available
  - Reliable and reproducible

Hodgkin Reed-Sternberg Cells Strongly Express CD30



Cytokine receptor CD30 selectively expressed in HRS cells

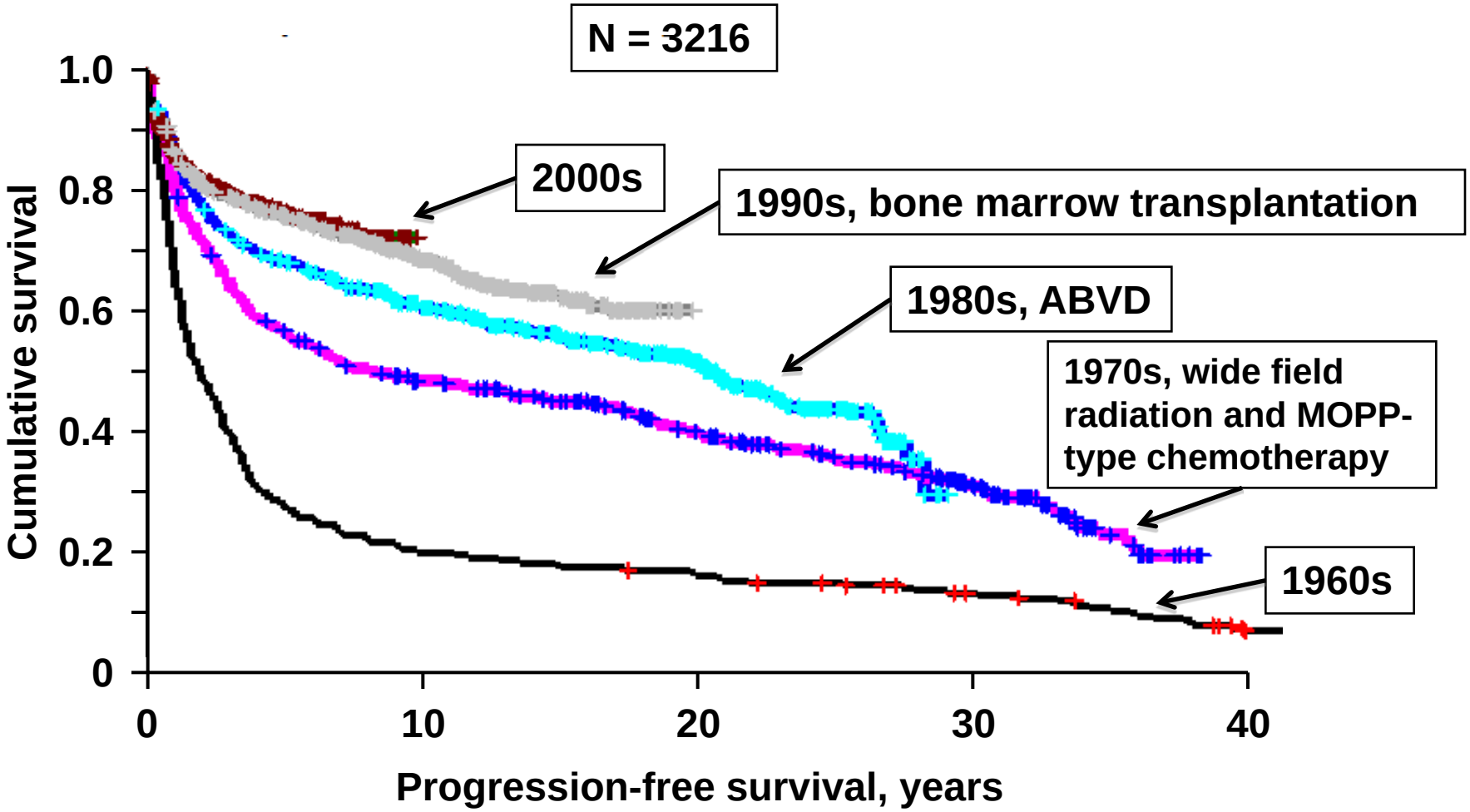
Hodgkin Lymphoma

- 2010 estimates[a]
  - 8490 new cases of HL were diagnosed
  - 1320 patients would die from their disease
- Median age at diagnosis is 38 years[b]
  - 90% of patients < 60 years
- Clinical presentation
  - Painless, enlarged lymph nodes commonly in the neck and thorax
  - 15% of patients with B symptoms (fever, night sweats, weight loss > 10%)

[a] Jemal A, et al. *CA Cancer J*. 2010;60(5):277-300; [b] National Cancer Institute. 2010. Surveillance, Epidemiology, and End Results (SEER) Program SEER*Stat Database: Incidence. http://seer.cancer.gov/canques/incidence.html.

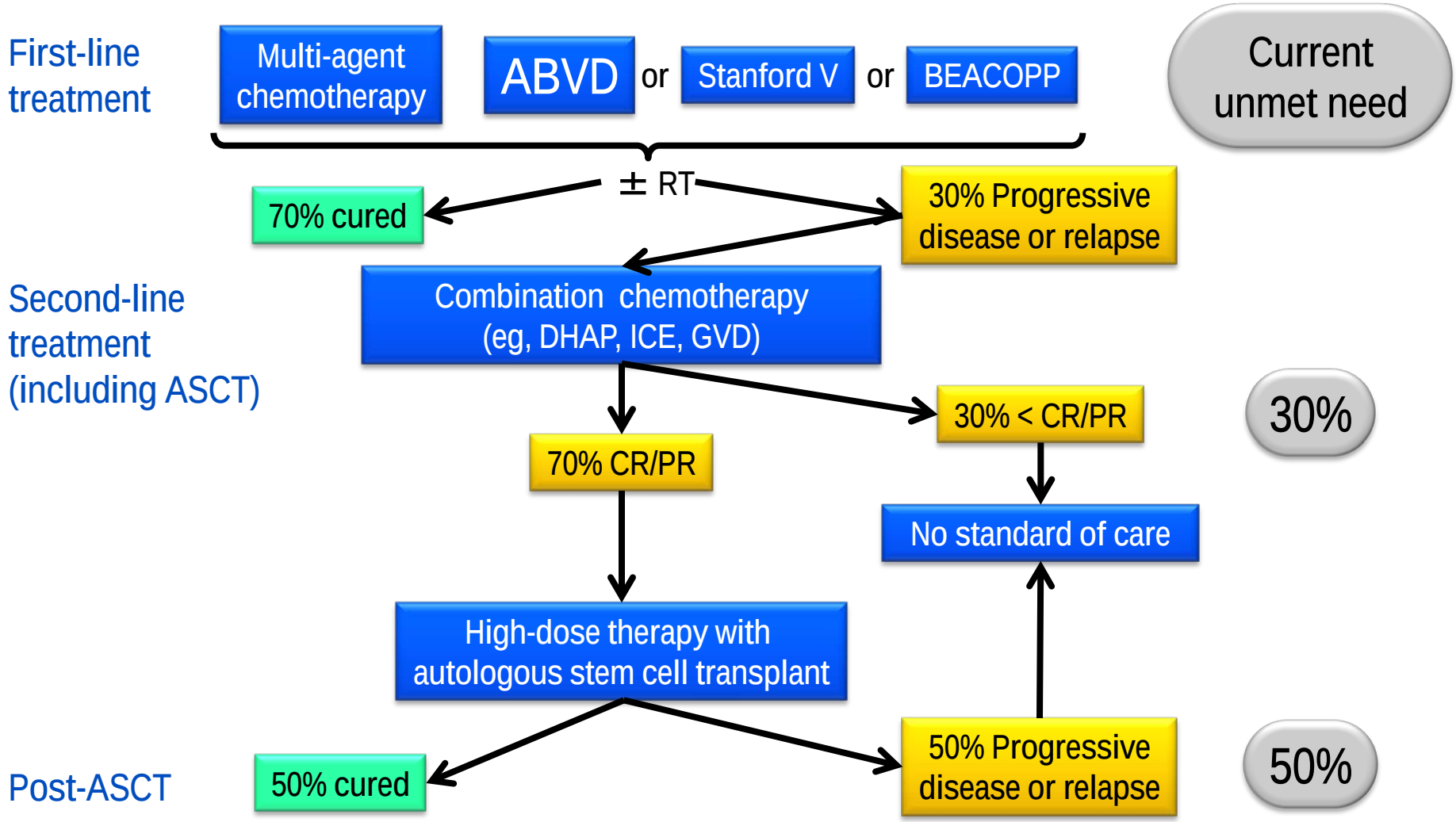
Progression-Free Survival by Decade of Diagnosis

Hodgkin Lymphoma



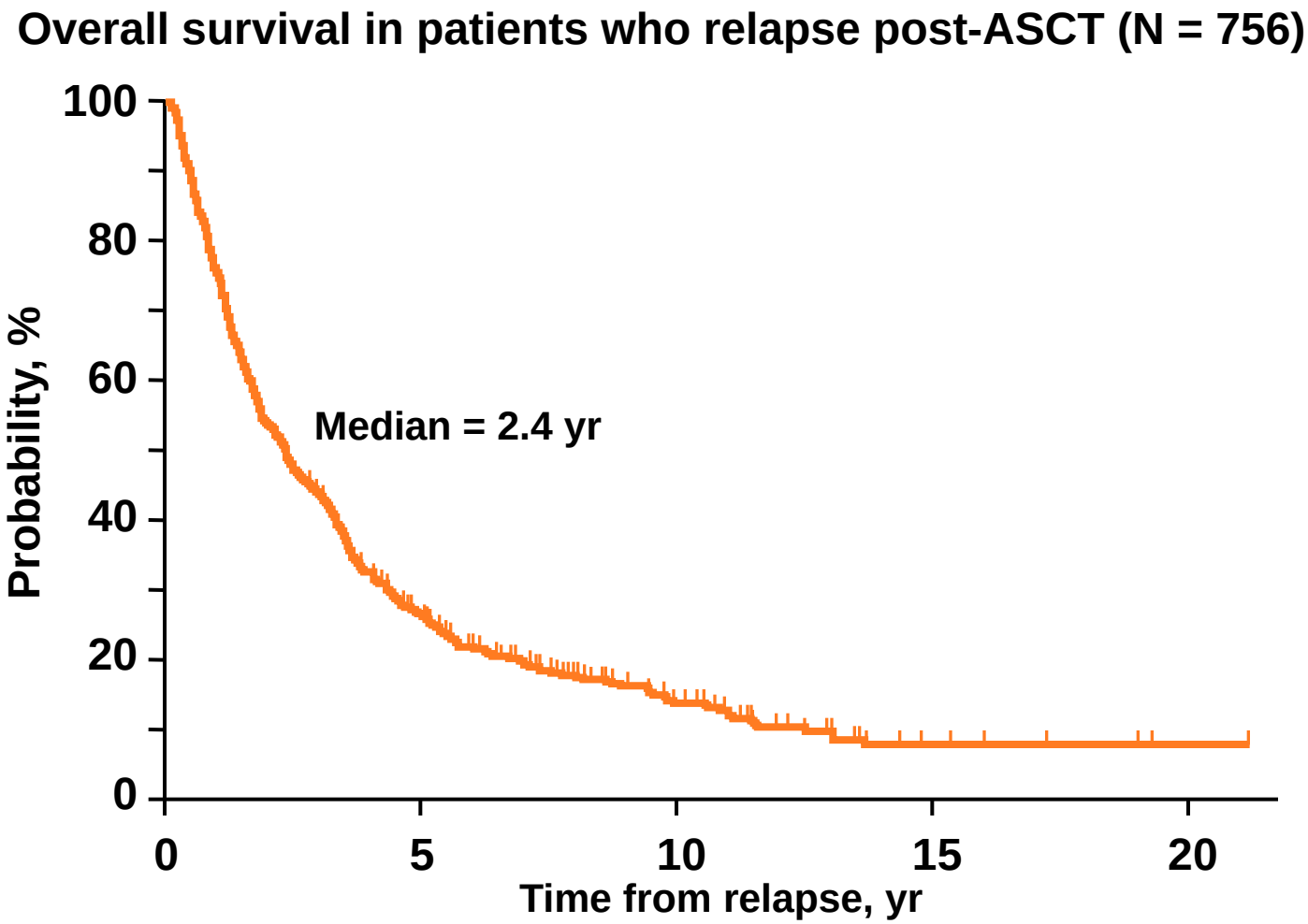
Data courtesy of Dr. Connors.

Treatment Algorithm for Advanced-Stage Hodgkin Lymphoma



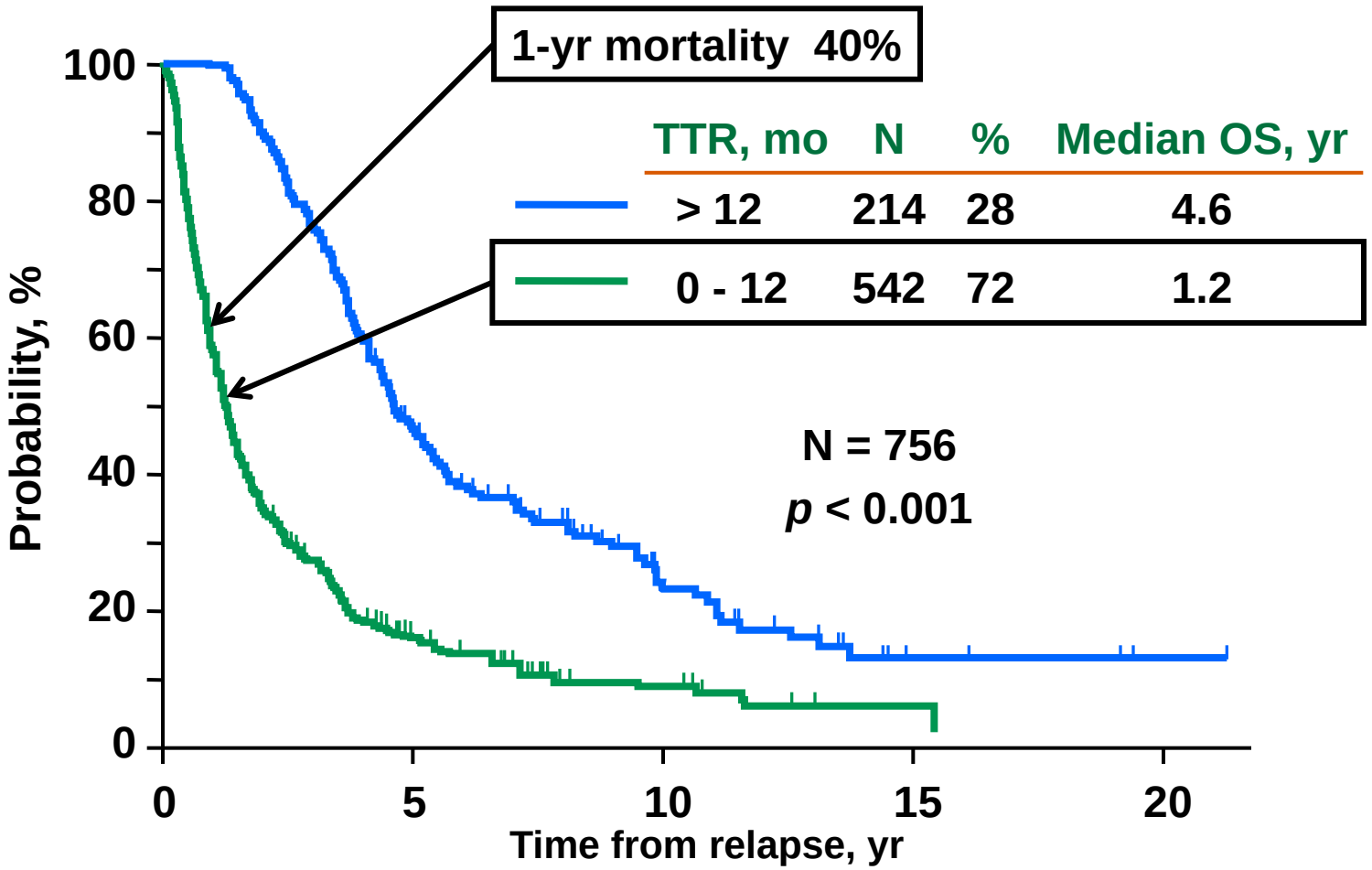
ASCT = Autologous stem cell transplant; CR = Complete remission; PR = Partial remission; RT = Radiation therapy.

Poor Survival in HL Patients Who Relapse After a Stem Cell Transplant



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

72% of Relapses After ASCT Occur in the First 12 Months and Have a Very Poor Prognosis



TTR = Time to relapse.

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

Treatment Options After Failure of ASCT

- No reliably curative options
  - Experimental allogeneic SCT
    - Applicable to small minority
    - Associated with marked toxicity
  - Curative wide-field radiation applicable to < 5%
- No approved treatment
- Pronounced unmet need

Treatment of Relapsed or Refractory Hodgkin Lymphoma

	All patients			Post-ASCT patients		
Agent	Evaluable patients, n	ORR, n (%)	CR, n (%)	Evaluable patients, n	ORR, n (%)	CR, n (%)
Vinblastine[a]	17	10 (59)	2 (12)	17	10 (59)	2 (12)
Vinorelbine[a]	22	11 (50)	3 (14)			
Rituximab[a]	22	5 (23)	1 (5)	18	5 (23)	1 (5)
Gemcitabine[a]	27	6 (22)	0	16	5 (31)	0
Vinorelbine + Gemcitabine[a]	8	6 (75)	4 (50)			
Rituximab + Gemcitabine[a]	33	16 (48)	5 (15)	18	11 (61)	
Bortezomib[a]	14	1 (7)	0	14	1 (7)	0
Bortezomib[a]	30	0	0	28		
Bortezomib[a]	12	0	0			
Gem, Vinor, Dox[b]	88	62 (70)	17 (19)	36	27 (75)	6 (17)
Panobinostat[c]	129	35 (27)	5 (4)	129	35 (27)	5 (4)

[a] Crump M. *Hema Am Soc Hematol Educ Prog.* 2008:326-333; [b] Bartlett NL, et al. *Ann Oncol*. 2007;18(6):1071-1079;
[c] Sureda A, et al. 52nd ASH Annual Meeting and Exposition. 2010. Abstract 169.

Key Concepts for Patients With Relapsed or Refractory Hodgkin Lymphoma

	Hodgkin lymphoma
Background	
• Malignant cells express CD30	~ 100 %
Disease impact	
• Not cured with current standard treatments	~ 25%
• Median OS	
– After failure of autologous transplant	29 mo
– Post-ASCT failure in < 1 year	14 mo
• Typical response to available treatment = partial	20% - 60%
• Typical duration of response	3 - 12 mo

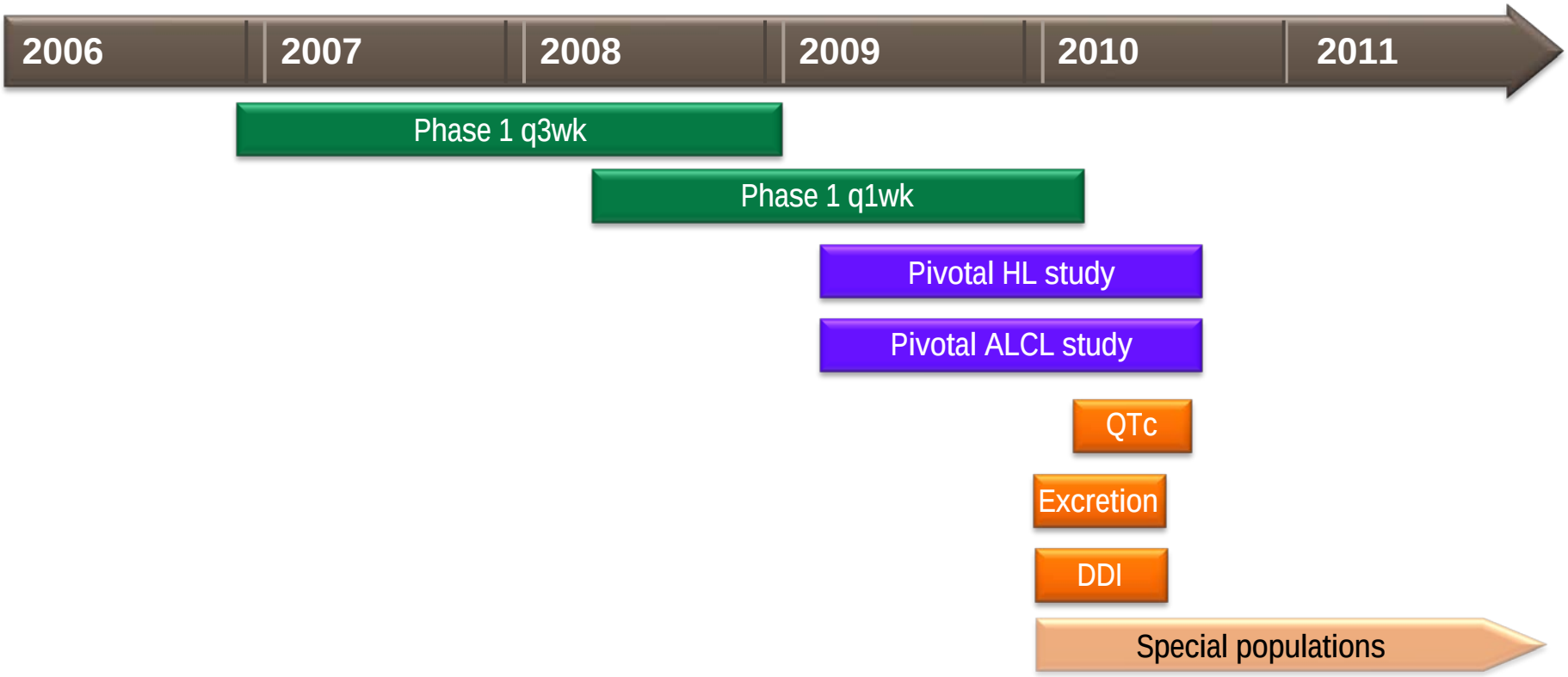
Brentuximab Vedotin Treatment of Patients With Hodgkin Lymphoma

Eric Sievers, MD

Vice President of Clinical Affairs
Seattle Genetics

SeattleGenetics®

Brentuximab Vedotin Clinical Development Program



Phase 1 First-in-Human Study

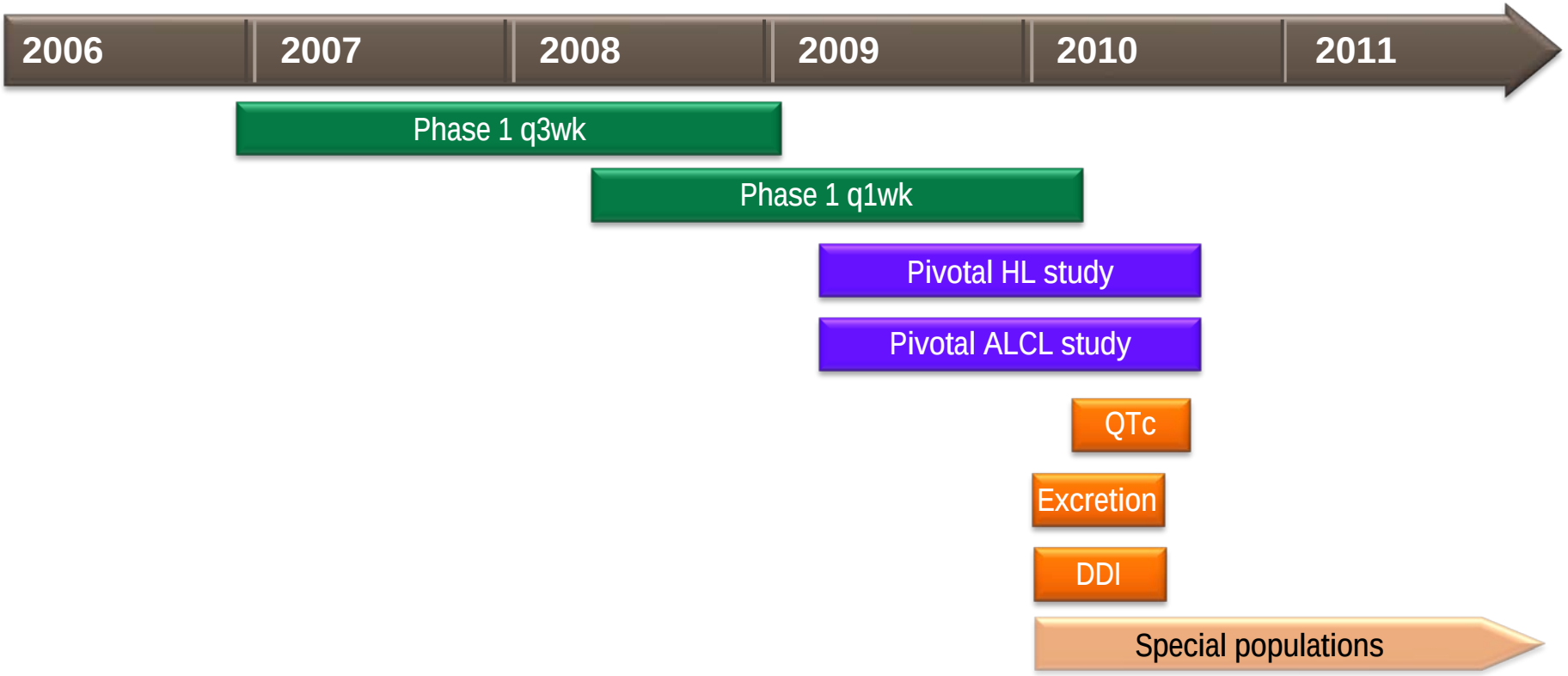
- Phase 1 dose-escalation study of brentuximab vedotin in patients with relapsed or refractory CD30+ hematological malignancies
- N = 45 enrolled at 4 US sites
  - Median age of 36 years
  - HL (n = 42), sALCL (n = 2), and angioimmunoblastic T-cell lymphoma (n = 1)
  - Median 3 prior regimens; prior ASCT in 73%
- Brentuximab vedotin was given intravenously every 3 weeks in escalating doses ranging from 0.1 to 3.6 mg/kg in successive cohorts
- 1.8 mg/kg every 3 weeks
  - Defined as MTD; also reasonably well-tolerated over months of continued therapy
  - Obtained durable complete remissions
  - Employed in the subsequent, paired registrational trials

[a] Younes A, et al. *N Engl J Med*. 2010;363(19):1812-1821.

Results
Phase 1 Program—Hodgkin Lymphoma

	Q 3 week trial n = 42	Q 1 week trial n = 38
Overall response rate	**36%**	**53%**
Complete remission rate	**21%**	**26%**
Median, months (min - max)		
Duration of overall response	**NE (0.6 - 19.4+)**	**4.8 (0.5+ - 17.3+)**
Duration of complete remission	**NE (1.4+ - 19.4+)**	**5.1 (0.5+ - 17.3+)**

Brentuximab Vedotin Clinical Development Program



Phase 2 Pivotal, Multicenter, Open-Label Trial Endpoints

- **Primary: Overall objective response rate (CR + PR)**
  - **Independent review facility**
  - **Revised response criteria for malignant lymphoma[a]**
- **Secondary**
  - **Efficacy**
    - **Duration of response**
    - **CR rate**
    - **PFS**
    - **OS**
    - **B symptom resolution**
  - **Safety**
    - **Adverse events**
    - **Laboratory abnormalities**

CR = Complete remission; PR = Partial remission; PFS = Progression-free survival; OS = Overall survival.

[a] Cheson BD, et al. *J Clin Oncol*. 2007;25(5):579-586.

2007 Revised Response Criteria for Malignant Lymphoma

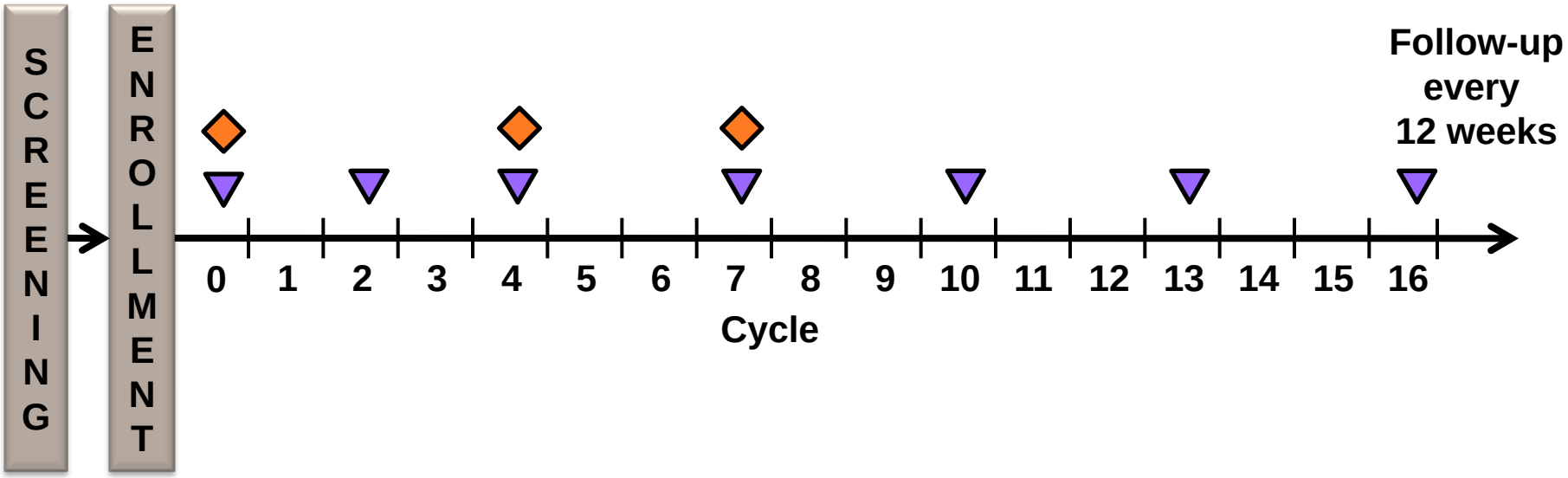
Response	Definition	Nodal lesions
CR	Disappearance of all evidence of disease	Residual mass of any size permitted if PET-negative
PR	Regression of measurable disease and no new sites	≥ 50% decrease in SPD of index lesions; 1 or more PET-positive at previously involved site
SD	Failure to attain CR/PR or PD	PET-positive at previously involved site and no new sites of disease
PD	Any new lesion or increase by ≥ 50% of previously involved sites from nadir	Progression of existing non-index lesions or ≥ 50% increase in SPD of index lesions or new lesion > 1.5 cm in any axis

CR = Complete remission; PR = Partial remission; SD = Stable disease; PD = Progressive disease; SPD = Sum of the products of the diameters.

Cheson BD, et al. *J Clin Oncol*. 2007;25(5):579-586.

Pivotal, Multicenter, Open-Label Trials of Brentuximab Vedotin

Brentuximab vedotin 1.8 mg/kg IV over 30 minutes every 3 weeks



▽ CT scan between Days 15 and 21 of cycle

◇ PET scan (no additional scans past Cycle 7 unless clinically indicated)

Key Eligibility Criteria
Hodgkin Lymphoma

- Relapsed or refractory, progressive HL
- CD30 expression confirmed centrally
- FDG-avid, CT-measurable disease ≥ 1.5 cm
- Prior ASCT was required
- Age ≥ 12 years
- ECOG performance status score 0 to 1

Statistical Considerations
Hodgkin Lymphoma

- Trial and analyses conducted under Special Protocol Assessment
- Primary statistical hypothesis: ORR 95% CI lower bound > 20%
  - Study size of 100 patients was chosen to allow evaluation of primary hypothesis
  - Observation of an ORR of 29% or greater would exclude a lower bound of 20%

ORR = Overall response rate.

Study Conduct and Oversight
Hodgkin Lymphoma

- Study steering committee guided design, conduct, and data interpretation
- Independent data monitoring committee actively evaluated for safety signals
- Independent response assessments
  - Prospectively rendered by central radiology blinded to clinical data
  - Overall assessment additionally integrated clinical data

Demographics and Baseline Characteristics

Hodgkin Lymphoma

	N = 102
Median age, yr (range)	31 (15 - 77)
Gender, n	48 M / 54 F
ECOG performance status score, %	
0	41
1	59
Refractory to front-line therapy, %	71
Refractory to most recent treatment, %	42
Median prior chemotherapy regimens, n (range)	3.5 (1 - 13)
Prior radiation, %	66
Prior ASCT, %	100
Relapsed ≤ 1 yr post-ASCT, %	71
Median time from ASCT to first post-transplant relapse, months (range)	6.7 (0 - 131)

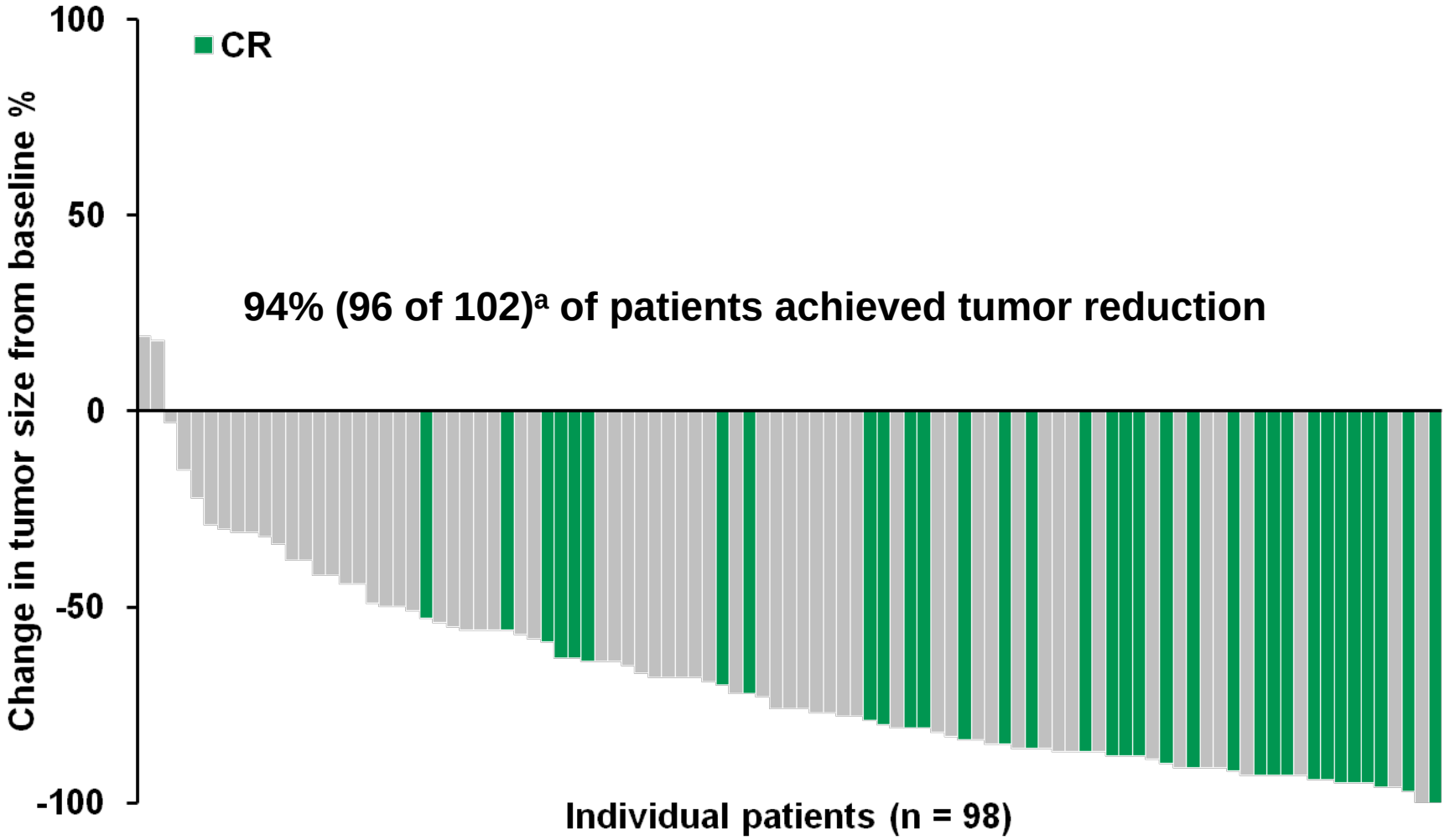
Response Results
Hodgkin Lymphoma

	N = 102
Overall response rate, % (95% CI)	75 (65, 83)
Complete remission, % (95% CI)	34 (24, 44)
Partial remission, %	40
Median, months (95% CI)	
Duration of overall response	6.7 (3.6, 14.8)
Duration of complete remission	20.5 (10.8, NE)
Progression-free survival	5.6 (5.0, 9.0)
Overall survival[a]	22.4 (21.7, NE)
B-symptom resolution, % (n/N)	77% (27/35)

NE = Not estimable.

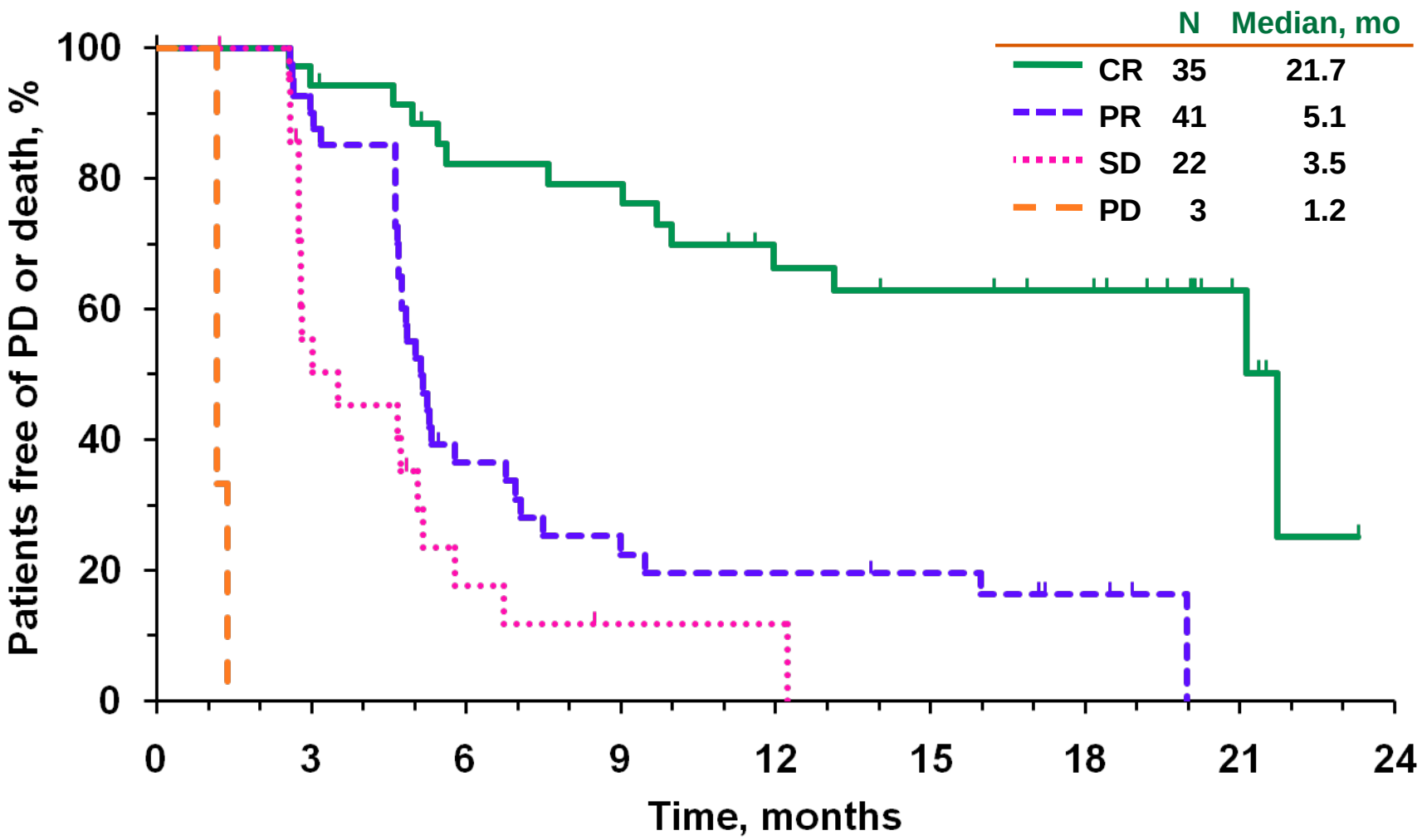
[a] 18-month overall survival estimated to be 80% (95% CI: 73%, 88%).

Maximum Tumor Reduction
Hodgkin Lymphoma

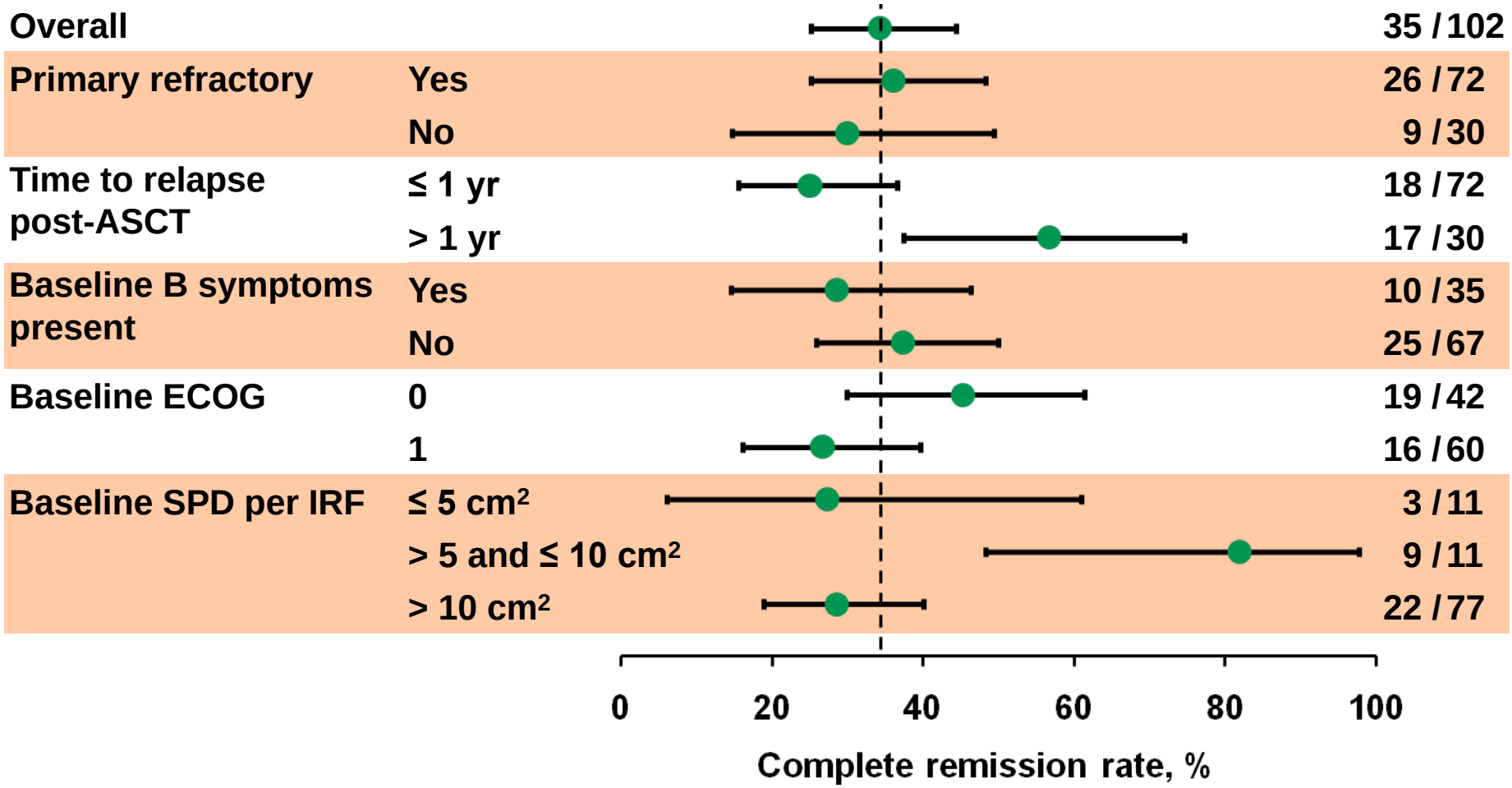


[a] 4 patients not included in analysis (3, no measurable lesions per IRF; 1, no post-baseline scans).

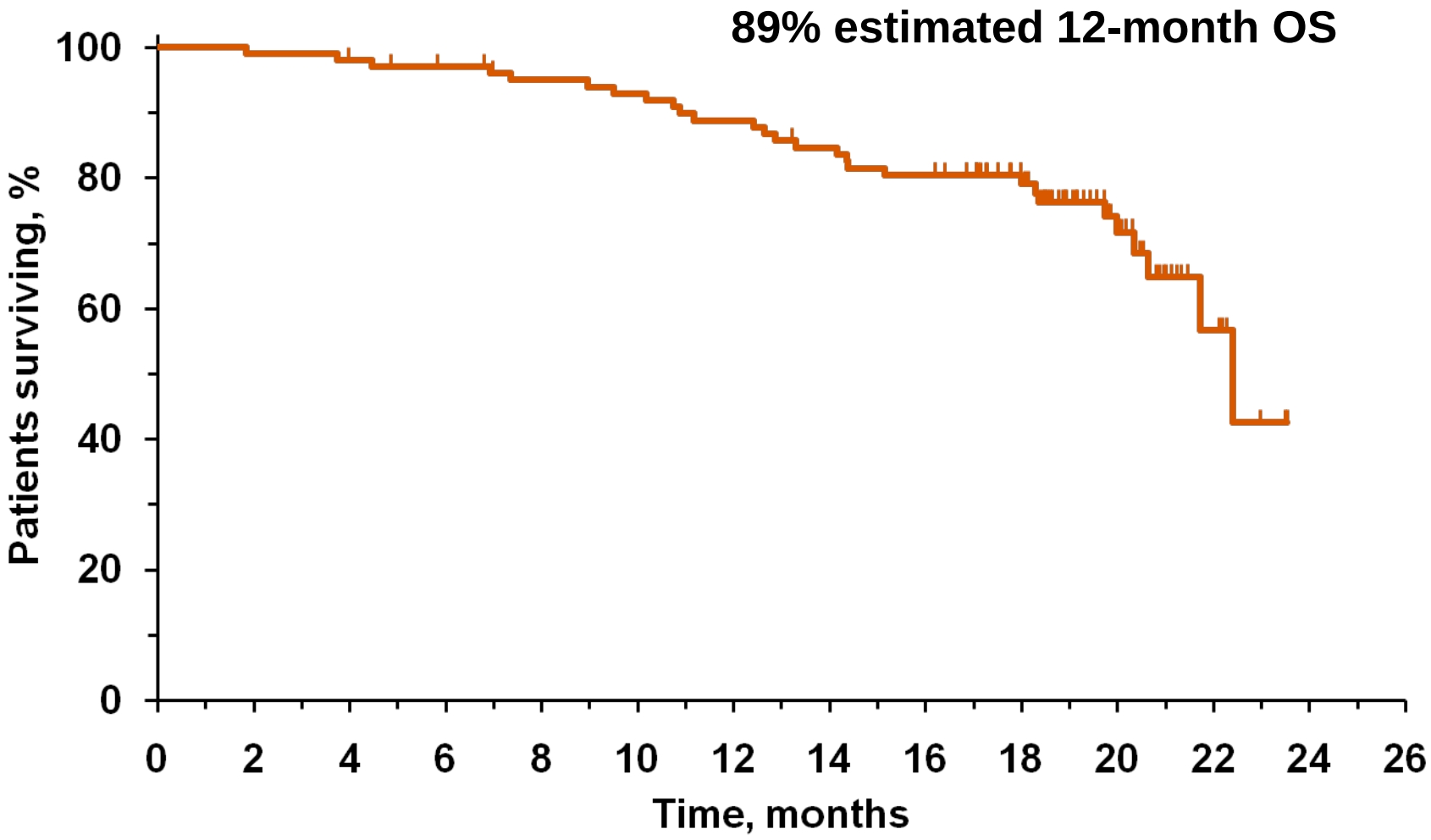
PFS by Best Clinical Response per IRF
Hodgkin Lymphoma



CR Rate Was Similar in All Patient Subsets
Hodgkin Lymphoma



Overall Survival
Hodgkin Lymphoma



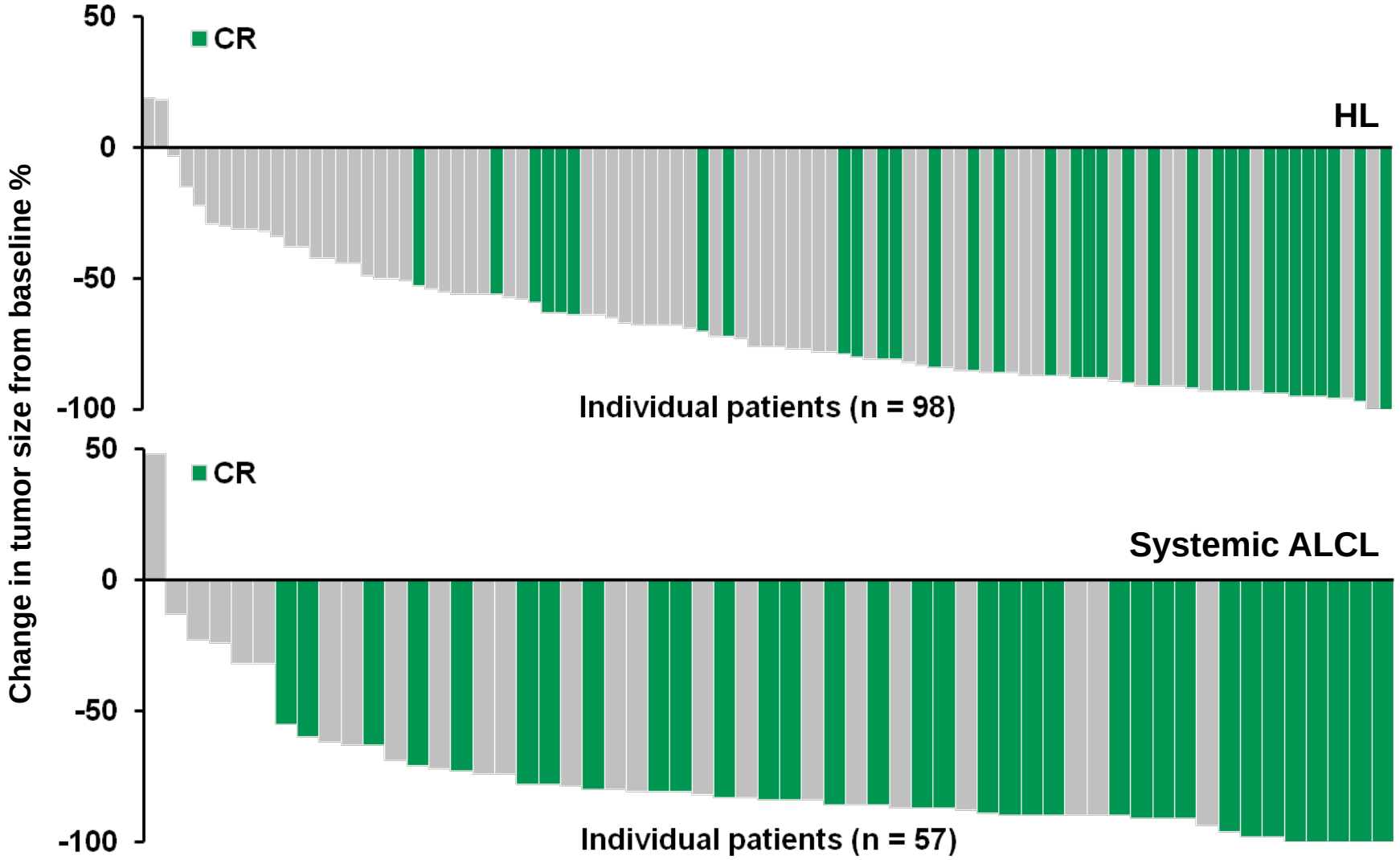
Consistent Response Rates
Pivotal Studies in Two CD30+ Lymphomas

Treatment response	HL patients N = 102	ALCL patients N = 58
Overall response rate, % (95% CI)	75 (65, 83)	86 (75, 94)
Complete remission, % (95% CI)	34 (25, 44)	57 (43, 70)
Median duration of response for CR patients, mo (95% CI)	20.5 (10.8, NE)	13.2 (10.8, NE)

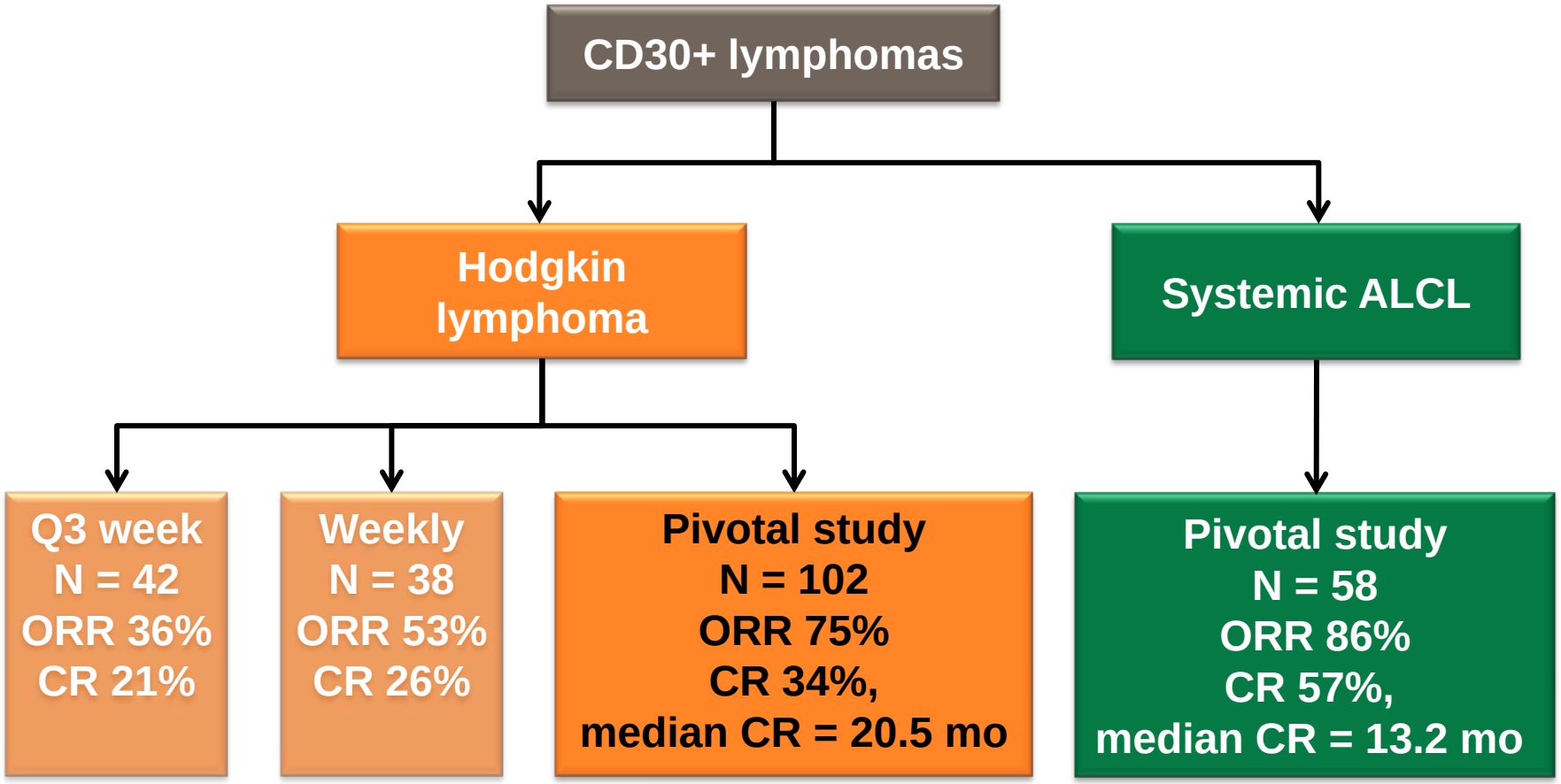
NE = Not estimable.

Consistent Tumor Reduction

Pivotal Studies in Two CD30+ Lymphomas



Durable Complete Remission Represents Clinical Benefit in CD30+ Lymphoma Patients



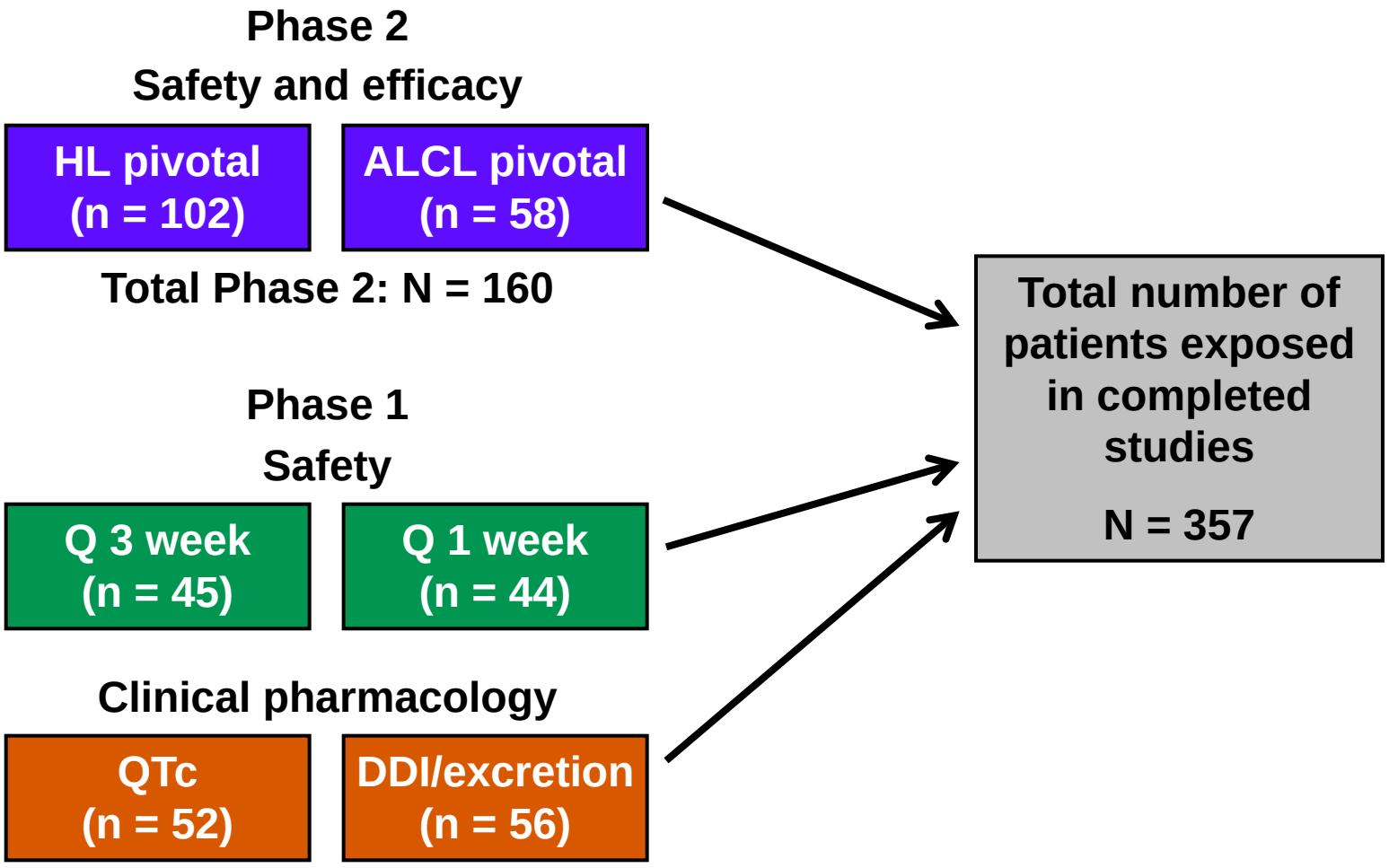
Brentuximab Vedotin Safety Profile

Tom Reynolds, MD, PhD

Chief Medical Officer
Seattle Genetics

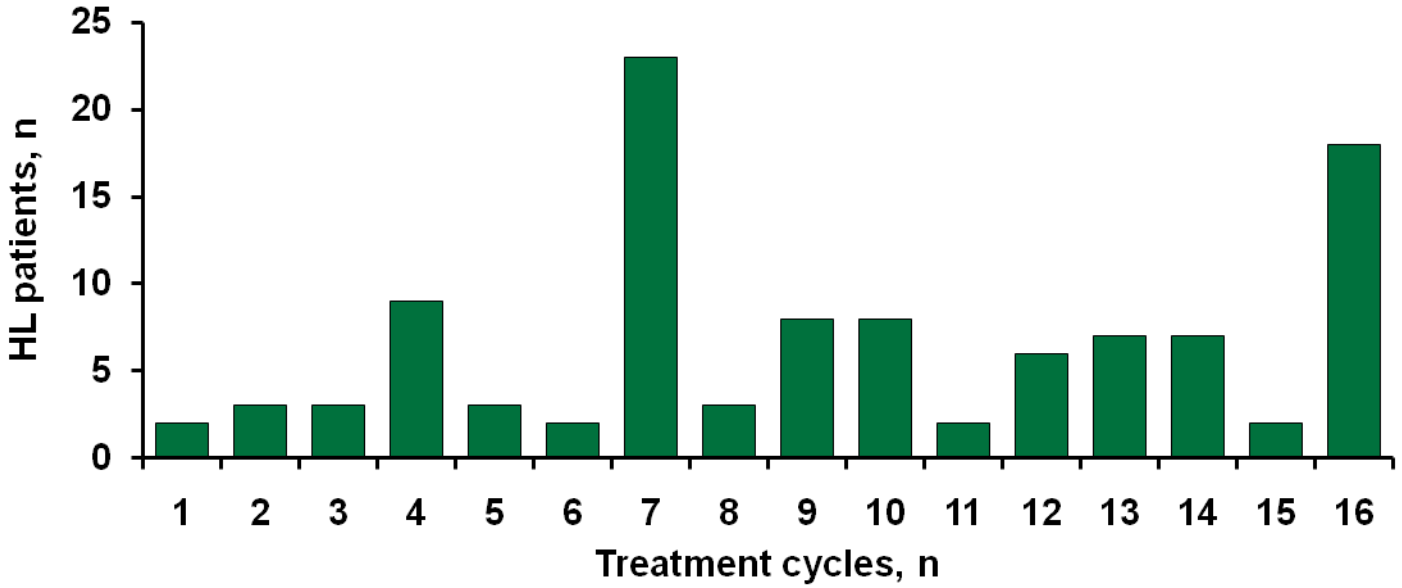
SeattleGenetics®

Safety Profile of Brentuximab Vedotin



Brentuximab Vedotin Exposure

Median treatment	HL patients n = 102	Total patients N = 160
Cycles, n (range)	9.0 (1 - 16)	7.0 (1 - 16)
Duration, mo (range)	6.2 (0.7 - 12.9)	5.5 (0.7 - 12.9)
Relative dose intensity, % (range)	96.0 (69 - 107)	97.3 (47 - 115)



Dose Modifications

- Dose modifications were prospectively defined in study protocols
- Patients could have their dose delayed up to 3 weeks or reduced to 1.2 mg/kg for AEs

Per-protocol and unplanned dose modifications	Patients, %	
	HL n = 102	Total N = 160
Dose reduction	11	10
Dose delay[a]	47	41
Dose adjustment due to an AE	12	8

[a] Only 8% of total doses were delayed due to an AE.

Patient Disposition

HL patients, N	
Enrolled, n	102
Received ≥ 1 dose, n	102

Reason for treatment discontinuation, %	
Completed treatment	18
Progressive disease	44
Adverse event	20
Investigator decision	12
Patient decision, non-AE	7

Adverse Events of Any Relationship Occurring in ≥ 20% of Phase 2 Patients

Preferred term	Patients, %	
	HL n = 102	Total N = 160
Peripheral sensory neuropathy	47	44
Fatigue	46	42
Nausea	42	41
Diarrhea	36	34
Pyrexia	29	31
Upper respiratory tract infection	37	28
Neutropenia	22	21
Vomiting	22	20

[a] Only 8% of total doses were delayed.

Adverse Events Grade 3-4 Occurring in ≥ 2% of Phase 2 Patients

	HL patients, % n = 102			Total patients, % N = 160		
Preferred term	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4
Peripheral sensory neuropathy	47	8	—	44	9	—
Fatigue	46	2	—	42	2	1
Diarrhea	36	1	—	34	2	—
Pyrexia	29	2	—	31	2	—
Neutropenia	22	14	6	21	13	7
Thrombocytopenia	8	6	2	10	7	3
Peripheral motor neuropathy	12	1	—	9	2	—

Total patients with any ≥ Grade 3 event = 55%

Summary of Deaths

	Patients, n	
	HL n = 102	Total N = 160
All deaths	13	25
Related to disease	10	18
Not related to disease	2	5
Disease relationship unknown	1	2
Deaths < 30 days of last dose	—	6

Special Safety Topics and Management of Toxicity

Peripheral Neuropathy AEs

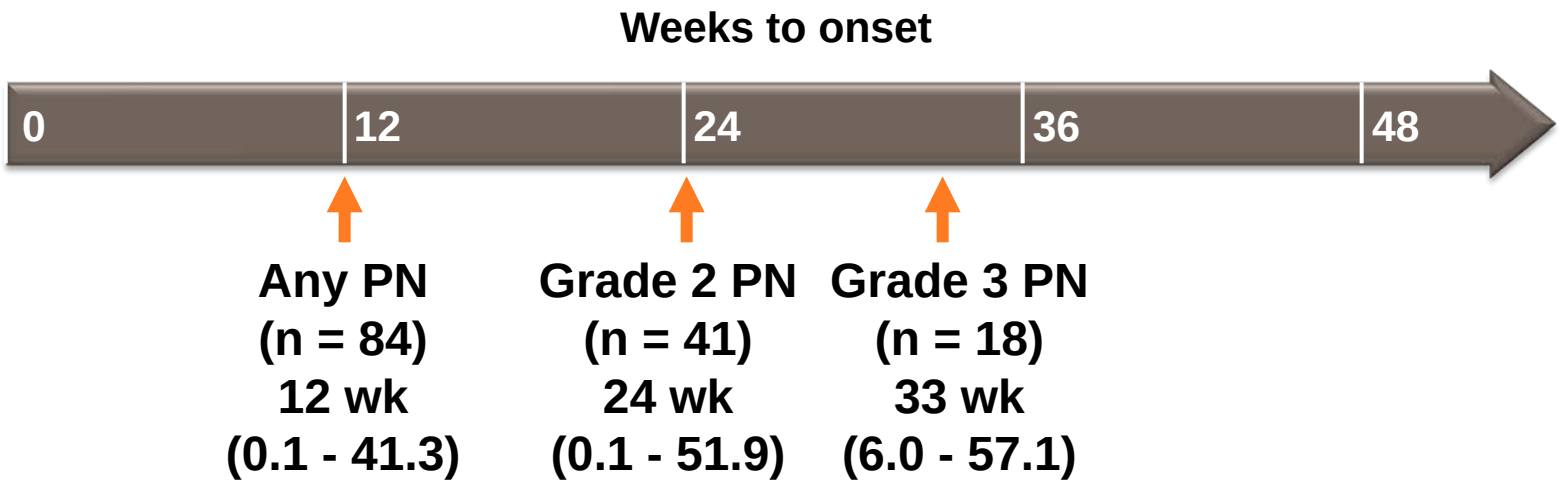
	HL patients, % n = 102		Total patients, % N = 160	
	Any grade	Grade 3	Any grade	Grade 3
Any PN SMQ AE[a]	55	11	53	11
Peripheral sensory neuropathy	47	8	44	9
Peripheral motor neuropathy	12	1	9	2
Paresthesia	4	—	4	—
Demyelinating polyneuropathy	2	2	1	1
Hypoesthesia	2	—	1	—
Muscular weakness	2	1	1	1
Neuralgia	—	—	1	—

SMQ = Standard MedDRA query.

[a] Events of any relationship occurring in > 1 patient.

Characterization of Treatment-Emergent Peripheral Neuropathy

Total Phase 2 Population



- Median time to complete or partial resolution: 6.6 wk (0.3, 54.4)
- Resolution: 62%
  - Complete: 31%
  - Partial: 31%

Dose Modifications in Patients With Grade 2 Neuropathy Can Reduce Worsening of Neuropathy

- Of patients with grade 2 neuropathy
  - 0/15 who had doses delayed had worsening
  - 2/10 who had dose reduction had worsening
  - 6/18 who had neither dose delays nor reductions had worsening
- Both dose delays and dose reductions appeared to be effective in reducing progression of Grade 2 neuropathy

Management of Peripheral Neuropathy

- Patients should be monitored for signs and symptoms of PN
- Neuropathy events
  - Primarily sensory
  - Appear to be associated with cumulative dosing
  - Largely reversible
- Patients experiencing new or worsening Grade 2 PN
  - Hold dosing until resolution to Grade 1 or baseline

  AND
  - Reduce dose to 1.2 mg/kg

Neutropenia Experience

Adverse event of neutropenia	HL patients n = 102	Total patients N = 160
≥ Grade 3	20%	20%
Median duration	8 days	8 days
Grade 4	6%	7%
Median duration	4 days	6 days
Any infections temporally associated with neutropenia/low neutrophils	33% (7/21)	39% (14/36)
Most < Grade 3, not serious		
Febrile neutropenia	—	—
Discontinuation due to neutropenia	—	—

Management of Neutropenia

- Prolonged (≥ 1 wk) cases of Grade 4 neutropenia can occur
- CBC should be monitored with each dose
- If Grade 3 or 4 neutropenia develops, manage according to institutional standards

Infusion-Related Reactions of Any Relationship Occurring in > 1 Patient

	Patients, %	
	HL n = 102	Total N = 160
Any infusion-related reaction	**12**	**11**
Chills	5	4
Nausea	4	3
Dyspnea	4	3
Pruritus	4	3
Cough	3	2
Dizziness	1	1
Erythema	2	1
Flushing	2	1
Pyrexia	1	1
Rash	1	1
Throat tightness	2	1
Vomiting	1	1

Management of Infusion-Related Reactions (IRR)

- Routine premedications not required
- In the event of IRR or anaphylaxis
  - Stop infusion
  - Institute appropriate medical management
  - Restart infusion (at a slower rate)
  - Premedication with subsequent infusions

Single-Event AEs

- Stevens-Johnson Syndrome (SJS)
  - HL patient receiving multiple medications including naproxen
  - Developed symptoms ~ 2 weeks after receiving his second dose of brentuximab vedotin
  - Patient discontinued treatment
  - Event resolved in less than 1 month
- Tumor Lysis Syndrome (TLS)
  - ALCL patient with bulky disease
  - Developed symptoms Day 1 of the Cycle 1 dose
  - Event was considered resolved 5 days after onset
  - Patient received a total of 8 cycles of treatment
  - Patient had a CR and went on to allogeneic transplant

Brentuximab Vedotin Has a Manageable Safety Profile

- Median duration of treatment: 6.2 months
- No treatment-related deaths
- Most common AE was peripheral neuropathy
  - Primarily Grade 1 and 2 sensory
  - Largely reversible
- Grade 3/4 hematologic toxicity was limited
- Low rate of infusion reactions observed (Grade 1/2)
- No evidence of cardiac, renal, or hepatic toxicity signals

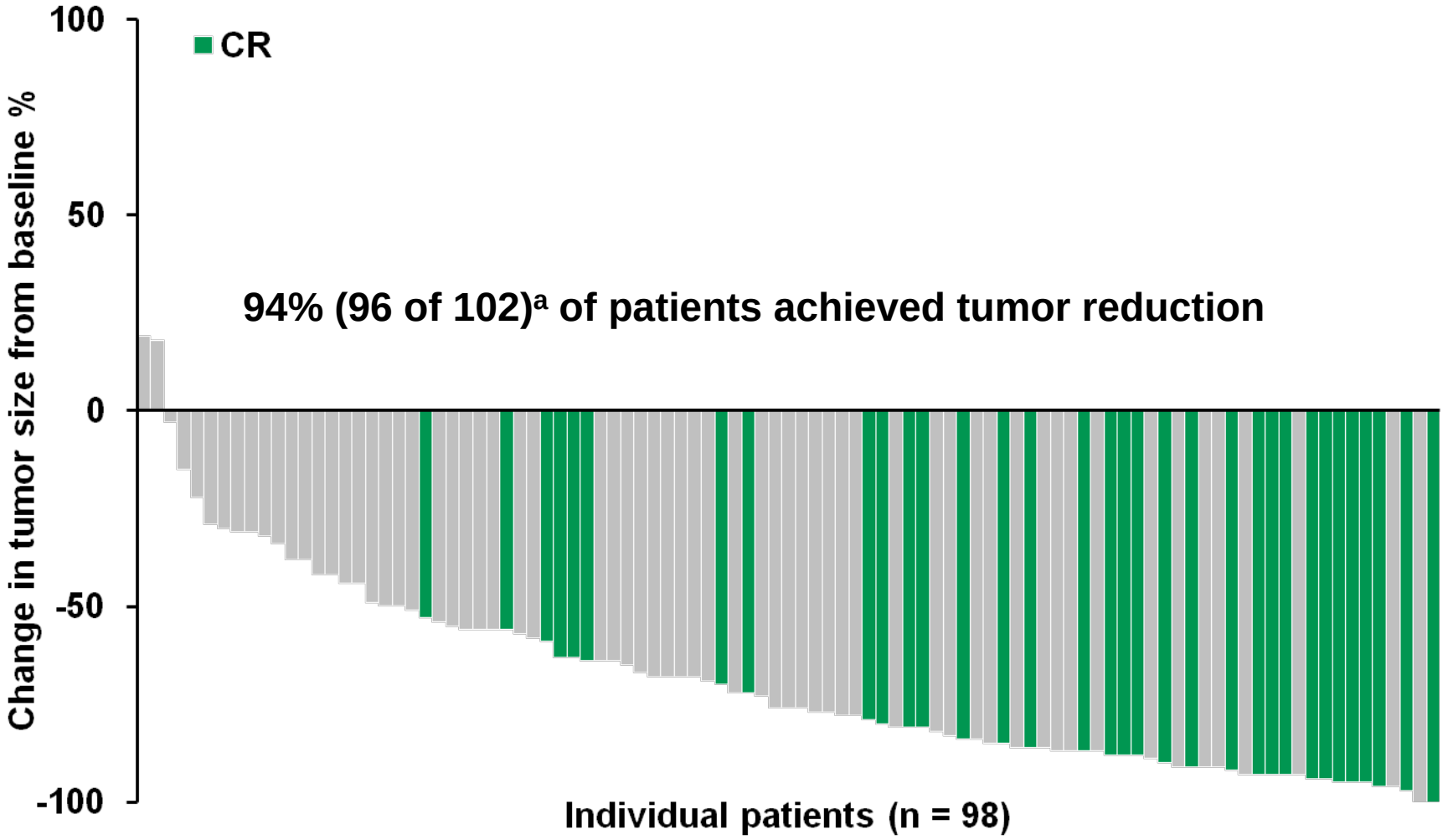
Brentuximab Vedotin
Hodgkin Lymphoma Benefit:Risk Profile

Joseph M. Connors, MD, FRCPC

Clinical Director, Centre for Lymphoid Cancer
British Columbia Cancer Agency
University of British Columbia

SeattleGenetics®

Benefit: Tumor Reduction



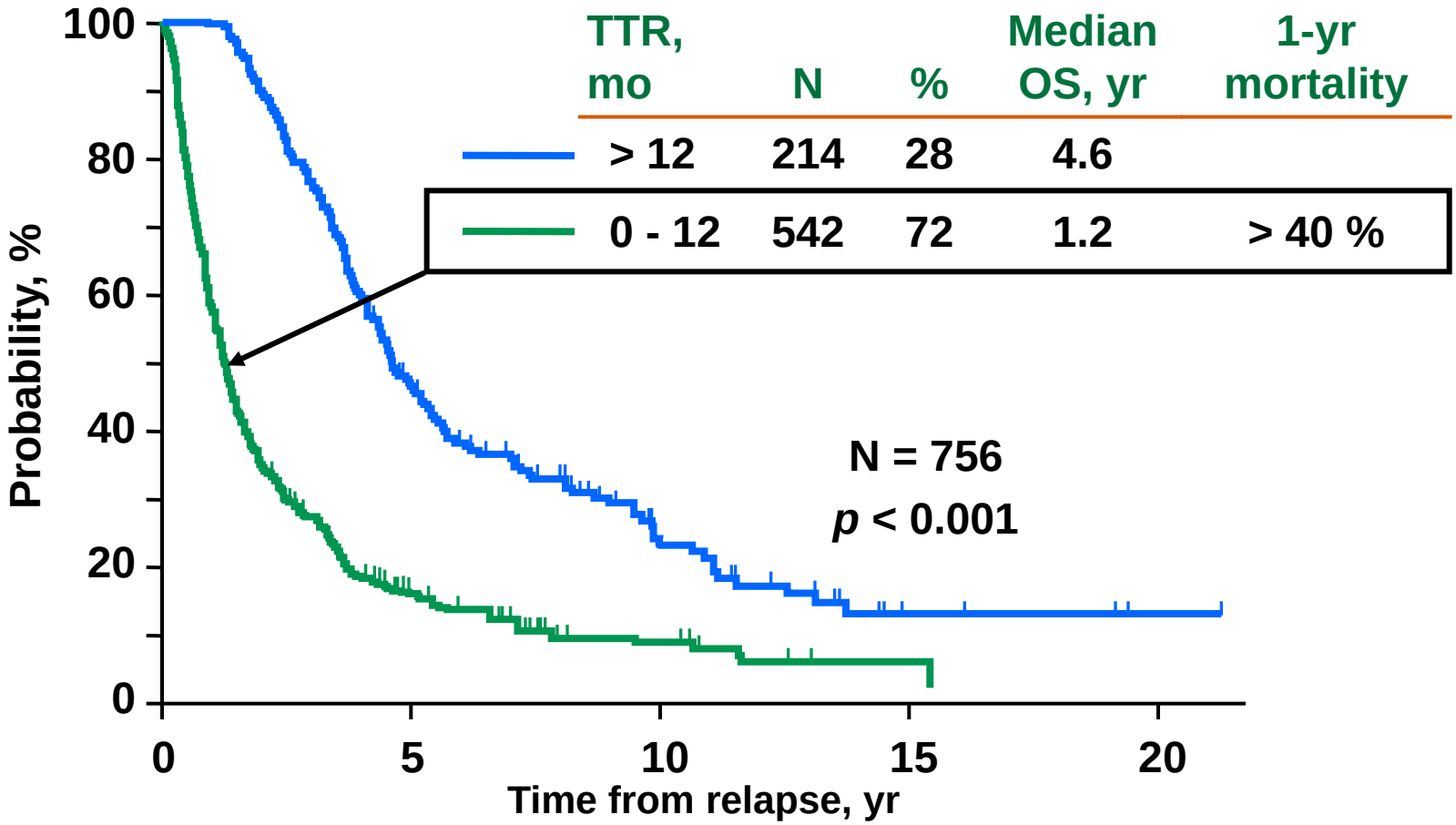
[a] 4 patients not included in analysis (3, no measurable lesions per IRF; 1, no post-baseline scans).

Benefit: Clinically Meaningful Results

	HL patients N = 102	ALCL patients N = 58
Treatment response		
Overall response rate	75%	86%
Complete remission (CR)	34%	57%
Median duration of CR, mo	20.5	13.2
Symptom resolution		
B symptom resolution	77% N = 35	82% N = 17

NE = Not estimable.

Benefit:
Population in Need: Post-transplant



TTR = Time to relapse.

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

Treatment of Relapsed or Refractory Hodgkin Lymphoma

Agent	All patients			Post-ASCT patients		
	Evaluable patients, n	ORR, n (%)	CR, n (%)	Evaluable patients, n	ORR, n (%)	CR, n (%)
Vinblastine[a]	17	10 (59)	2 (12)	17	10 (59)	2 (12)
Vinorelbine[a]	22	11 (50)	3 (14)			
Rituximab[a]	22	5 (23)	1 (5)	18	5 (23)	1 (5)
Gemcitabine[a]	27	6 (22)	0	16	5 (31)	0
Vinorelbine + Gemcitabine[a]	8	6 (75)	4 (50)			
Rituximab + Gemcitabine[a]	33	16 (48)	5 (15)	18	11 (61)	
Bortezomib[a]	14	1 (7)	0	14	1 (7)	0
Bortezomib[a]	30	0	0	28		
Gem, Vinor, Dox[b]	88	62 (70)	17 (19)	36	27 (75)	6 (17)
Panobinostat[c]	129	35 (27)	5 (4)	129	35 (27)	5 (4)
Brentuximab vedotin	**102**	**77 (75)**	**35 (34)**	**102**	**77 (75)**	**35 (34)**

[a] Crump M. *Hema Am Soc Hematol Educ Prog.* 2008:326-333; [b] Bartlett NL, et al. *Ann Oncol*. 2007;18(6):1071-1079; [c] Sureda A, et al. 52nd ASH Annual Meeting and Exposition. 2010. Abstract 169.

Benefit: Risk Ratio
Relapsed/Refractory Hodgkin Lymphoma

Need

- 50% relapse despite ASCT
- 72% of relapses occur in less than 1 yr of ASCT
  - ~ 40% 1-yr mortality rate
- All patients become markedly symptomatic
- Available off-label remedies ➔ short-term benefit in minority of patients
- High-quality response ➔ opportunity for potentially curative treatment

Risk

- Peripheral neuropathy
  - Any grade 55%
  - Grade 3 11%
- Transient grade 3/4 neutropenia 20%
- Infusion reactions 12%

Benefit

- ORR 75%
- CR 34%
- CR duration 20.5 months
- Potential to make eligible for transplant

Supportive Slides

Statistical Methods—Stratification
AETHERA

- Best clinical response achieved after completion of salvage therapy prior to ASCT
  - CR
  - PR
  - SD
- Prior disease status
  - Refractory
  - Relapsed < 12 months from the end of frontline therapy
  - Relapsed ≥ 12 months from the end of frontline therapy

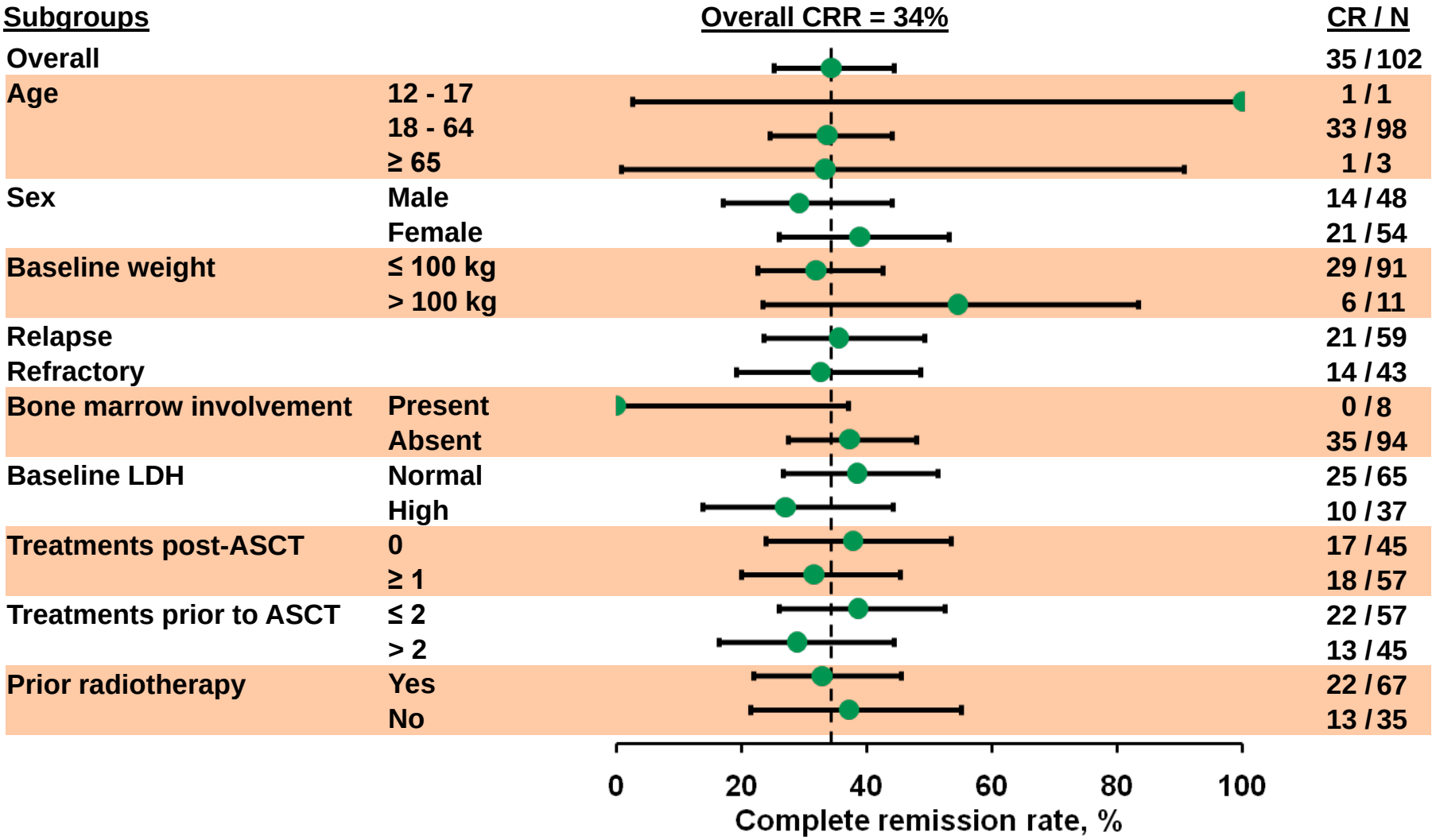
Brentuximab Vedotin Studies Ongoing and in Development

Indication	Study description	Ph 1	Ph 2	Ph 3
HL	AETHERA—post-ASCT, high-risk HL (placebo controlled)			X
	Combination chemo + brentuximab vedotin in front-line HL	X		
	Combination chemo + brentuximab vedotin in front-line HL			X
ALCL	Combination chemo + brentuximab vedotin in front-line sALCL	X		
	Combination chemo + brentuximab vedotin in front-line sALCL			X
CD30+ malignancies	Re-treatment		X	
	Cardiac safety (primary data complete)	X		
	Drug-drug interaction/Special populations	X		
	CD30+ NHL		X	
	CD30+ non-lymphomatous malignancies		X	
CTCL	Single agent vs physicians choice in CD30+ CTCL			X

Open In Development

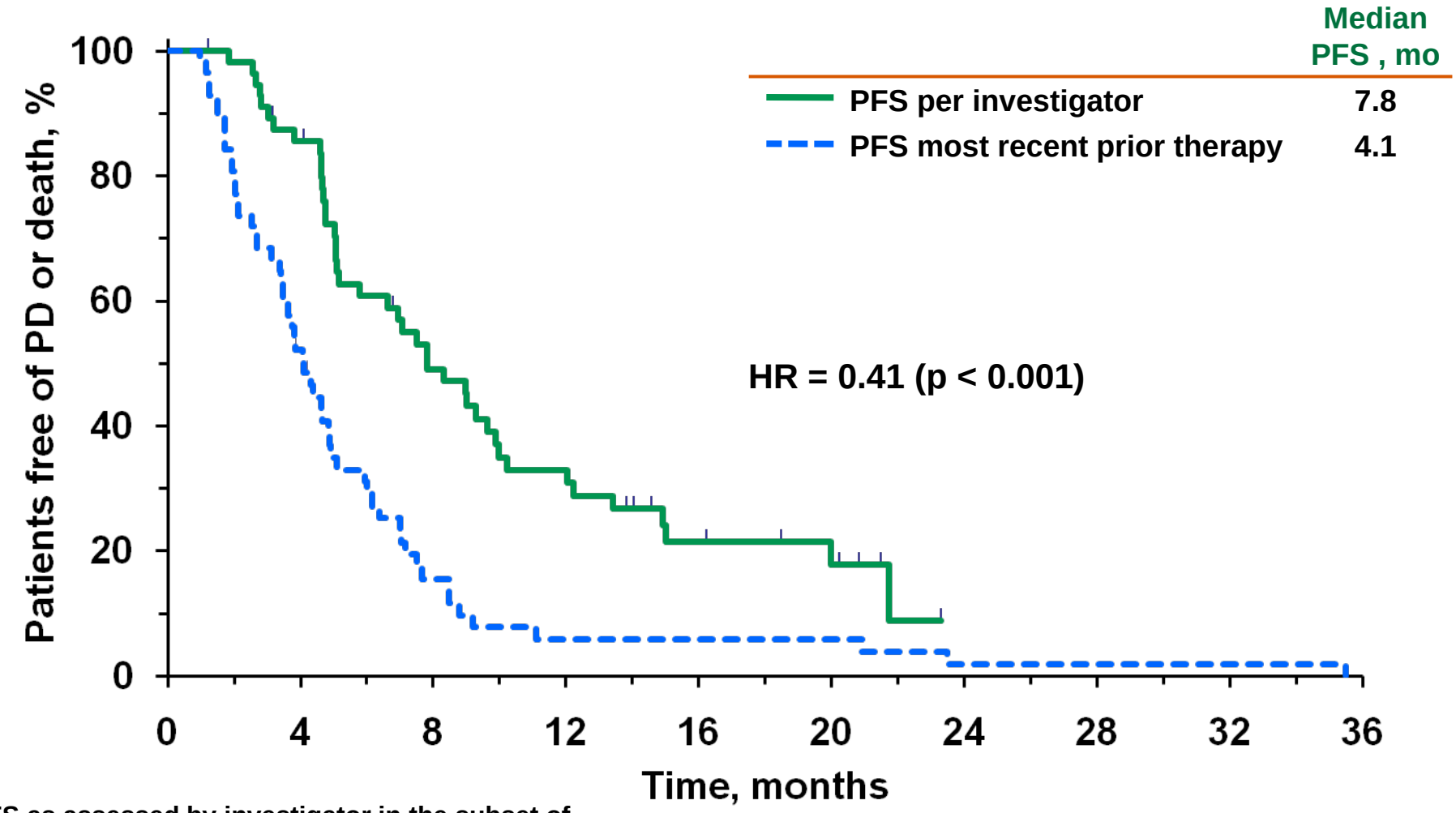
Complete Remissions by Additional Subgroups—March 2011

Hodgkin Lymphoma



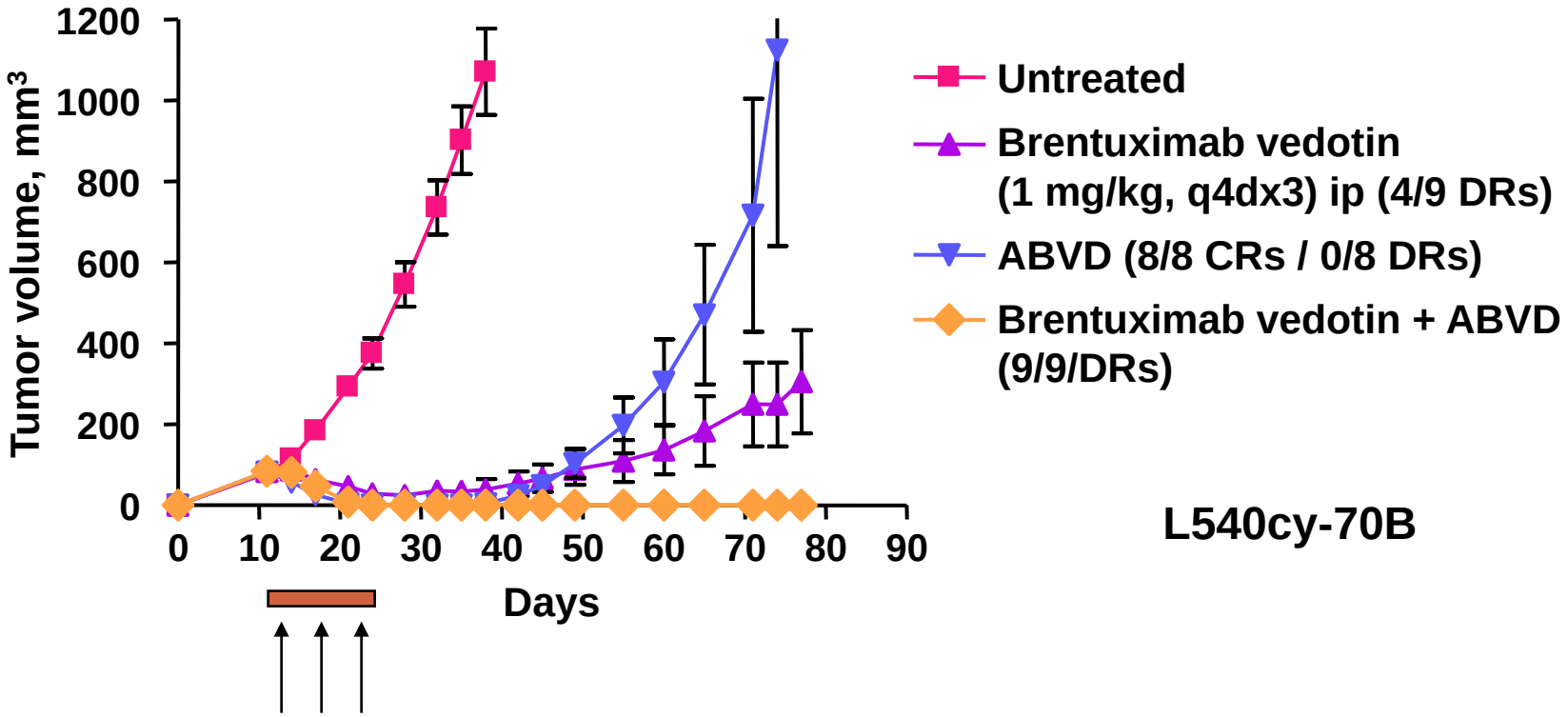
PFS[a]: Brentuximab Vedotin vs Last Prior Post-ASCT Therapy—March 2011

Hodgkin Lymphoma



[a] PFS as assessed by investigator in the subset of patients (n = 57) who received systemic therapy post-ASCT and prior to brentuximab vedotin.

Combination of Brentuximab Vedotin With ABVD Provides Better Efficacy Than Either Agent Alone



ABVD = Doxorubicin (1 mg/kg, q4dx3) iv; bleomycin (7.5 u/kg, q4dx3) ip; vinblastine (0.015 mg/kg q4dx3) ip; dacarbazine (20 mg/kg, q3dx4) ip.

Best Clinical Response by Immunogenicity Status in Baseline Negative Patients

Phase 2 Population

	HL patients, n (%) n = 96		
	Negative n = 64	Transient positive n = 24	Persistent positive n = 7
Objective response rate (CR + PR)	49 (77)	16 (67)	6 (86)
Disease control rate (CR + PR + SD)	63 (98)	22 (92)	7 (100)

	ALCL patients[a], n (%) N = 54		
	Negative n = 32	Transient positive n = 18	Persistent positive n = 3
Objective response rate (CR + PR)	28 (88)	15 (83)	3 (100)
Disease control rate (CR + PR + SD)	29 (91)	16 (89)	3 (100)

[a] Independent review facility assessment per Revised Response Criteria for Malignant Lymphoma.