Camidanlumab tesirine: updated efficacy and safety in an open-label, multicenter, phase 2 study of patients with relapsed or refractory classical Hodgkin lymphoma (R/R cHL)

Carmelo Carlo-Stella[1]*, Stephen Ansell[2], Pier Luigi Zinzani[3], John Radford[4], Kami Maddocks[5], Antonio Pinto[6], Graham P. Collins[7], Veronika Bachanova[8], Nancy Bartlett[9], Isabelle Bence-Bruckler[10], Mehdi Hamadani[11], Justin Kline[12], Jiri Mayer[13], Kerry J. Savage[14], Ranjana Advani[15], Paolo Caimi[16], René-Olivier Casasnovas[17], Tatyana Feldman[18], Brian Hess[19], Mariana Bastos-Oreiro[20], Sunil Iyengar[21], Sandy Eisen[22†], Yanina Negievich[22], Luqiang Wang[23], Jens Wuerthner[22], Alex F. Herrera[24]

[1]Humanitas University, Department of Oncology and Hematology, IRCCS Humanitas Research Hospital, Milano, Italy; [2]Mayo Clinic, Division of Hematology, Rochester, Minnesota, USA; [3]Institute of Hematology "Seràgnoli" University of Bologna, Bologna, Italy; [4]NIHR Clinical Research Facility, the Christie NHS Foundation Trust and University of Manchester, Manchester Academic Health Science Centre, Manchester, UK; [5]Ohio State University Medical Center, Division of Hematology, Columbus, Ohio, USA; [6]Istituto Nazionale Tumori - Fondazione G. Pascale, IRCCS, Naples, Italy; [7]NIHR Oxford Biomedical Research Centre, Oxford Cancer and Haematology Centre, Churchill Hospital, Oxford, UK; [8]Division of Hematology, Oncology, and Transplantation, University of Minnesota, Minneapolis, Minnesota, USA; [9]Washington University School of Medicine in St. Louis, Division of Oncology, St. Louis, Missouri, USA; [10]The Ottawa Hospital-General Campus, Ottawa-Hospital General Campus, Ottawa, Canada; [11]BMT & Cellular Therapy Program, Department of Medicine, Medical College of Wisconsin, Milwaukee, WI, USA; [12]The University of Chicago, Department of Medicine, Chicago, Illinois, USA; [13]University Hospital and Masaryk University, Brno, Czech Republic; [14]BC Cancer and University of British Columbia, Department of Medical Oncology, Vancouver, British Columbia, Canada; [15]Division of Oncology, Department of Medicine, Stanford University, Stanford, CA, USA; [16]Cleveland Clinic/Case Comprehensive Cancer Center, Cleveland, OH, USA; [17]Department of Hematology, University Hospital F. Mitterrand and Inserm UMR 1231, Dijon 21000, France; [18]John Theurer Cancer Center, Hackensack Meridian Health, Hackensack, NJ, USA; [19]Division of Hematology and Medical Oncology, Department of Medicine, Medical University of South Carolina, Charleston, SC, USA; [20]Haematology Department, Gregorio Marañón Health Research Institute, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [21]Royal Marsden Hospital, London, UK; [22]ADC Therapeutics SA, Epalinges, Switzerland; [23]ADC Therapeutics America, Inc., Murray Hill, New Jersey, USA; [24]City of Hope Comprehensive Cancer Center, Department of Hematology & Hematopoietic Cell Transplantation, Duarte, California, USA

*Presenting author; †Current affiliation: CNS Consult Ltd, Hertfordshire, England, UK

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Introduction

There are limited treatment options available for patients with R/R cHL who are refractory to or relapse following BV and PD-1 inhibitor therapy[1-2]

Camidanlumab tesirine (Cami) is an antibody drug conjugate comprising a human IgG1 anti-CD25 monoclonal antibody conjugated to a PBD dimer[3]

In a phase 1 trial in patients with lymphoma, including patients with cHL, Cami demonstrated encouraging antitumor activity and manageable toxicity[3]

Prior results of the phase 2 study evaluating Cami monotherapy in patients with R/R cHL showed an ORR of 66.3%, with a CRR of 27.7% (presented at ICML 2021)[4]

Here, we present updated efficacy and safety data from the phase 2 study (NCT04052997)

BV, brentuximab vedotin; cHL, classical Hodgkin lymphoma; CRR, complete response rate; Ig, immunoglobulin; PBD, pyrrolobenzodiazepine; ORR, overall response rate; PD-1, programmed cell death protein 1; R/R, relapsed or refractory.

1. Tarekegn K, et al. *World J Clin Oncol.* 2021;12(4):81-84; 2. Epperla N and Hamadani M. *Hematology Am Soc Hematol Educ Program.* 2021;(1):247-253. 3. Hamadani M, et al. *Lancet Oncol.* 2021;8(6):e433-e445. 4. Zinzani et al. Presented at: 2021 International Conference on Malignant Lymphoma; June 18-22, 2021; Virtual.

Study Design and Methods

Ongoing, Phase 2, single-arm, multicenter, open-label study in patients with R/R cHL[a]

30-minute IV infusion of Cami on Day 1 of each 3-week cycle

- Primary endpoint: ORR (per 2014 Lugano classification) assessed by central review
- Secondary endpoints: DoR, PFS, safety (frequency and severity of adverse events)
- As of November 1, 2021, enrollment was complete **(N=117)**

[a] Primary analyses of efficacy and safety in the all-treated population, defined as all patients who received ≥1 dose of Cami; [b] Or until discontinuation due to disease progression, unacceptable toxicity, or other reasons. Patients deriving clinical benefit at 1 year may be able to continue treatment on a case-by-case basis.
Cami, camidanlumab tesirine; cHL, classical Hodgkin lymphoma; DoR, duration of response; IV, intravenous; ORR, overall response rate; PFS, progression-free survival; R/R, relapsed or refractory.

Key Inclusion and Exclusion Criteria

Inclusion Criteria

- Male or female
- ≥18 years (≥16 years in US)
- Pathologic diagnosis of cHL
- Patients with R/R cHL who received ≥3 prior lines of systemic therapy (or ≥2 lines if ineligible for HSCT)
- Prior treatment with BV and PD-1 blockade therapy
- Measurable disease (2014 Lugano classification)
- Eastern Cooperative Oncology Group performance status score of 0–2
- Adequate organ function

Exclusion Criteria

- Allogeneic/autologous HSCT ≤60 days before start of Cami treatment
- History of neuropathy considered of autoimmune origin (e.g., polyradiculopathy including GBS and myasthenia gravis) or other CNS autoimmune disease, such as poliomyelitis or MS
- Recent infection (<4 weeks of Cycle 1, Day 1) considered caused by pre-specified pathogens
- HIV, HBV, or HCV infection needing antiviral therapy/prophylaxis
- Clinically significant third-space fluid accumulation (i.e., ascites requiring drainage, or pleural effusion requiring drainage or associated with shortness of breath)

BV, brentuximab vedotin; cHL, classical Hodgkin lymphoma; CNS, central nervous system; GBS, Guillain-Barré syndrome; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HSCT, hematopoietic stem cell transplantation; MS, multiple sclerosis; PD-1, programmed cell death protein 1; R/R, relapsed or refractory.

Baseline Characteristics

Characteristic	Total (N=117)
Sex, n (%)	
Female	44 (37.6)
Male	73 (62.4)
Age, median (Min, Max)	37 (19, 87)
ECOG score, n (%)	
0	64 (54.7)
1	47 (40.2)
2	6 (5.1)
Disease stage (Ann Arbor criteria)[1], n (%)	
I	1 (0.9)
II	22 (18.8)
III	25 (21.4)
IV	68 (58.1)
Missing	1 (0.9)

Characteristic	Total (N=117)
Prior systemic therapies, n (%)	
≤3 prior lines	5 (4.3)
4 prior lines	18 (15.4)
5 prior lines	22 (18.8)
>5 prior lines	72 (61.5)
Number of prior systemic therapies, median (min, max)[a]	**6 (3-19)**
Prior HSCT, n (%)	
Autologous	59 (50.4)
Allogeneic	3 (2.6)
Both	12 (10.3)
Disease status after first-line systemic therapy, n (%)	
Relapsed	79 (67.5)
Refractory	29 (24.8)
Other[b]	9 (7.7)
Disease status after last-line systemic therapy, n (%)	
Relapsed	37 (31.6)
Refractory	66 (56.4)
Other[b]	14 (12.0)

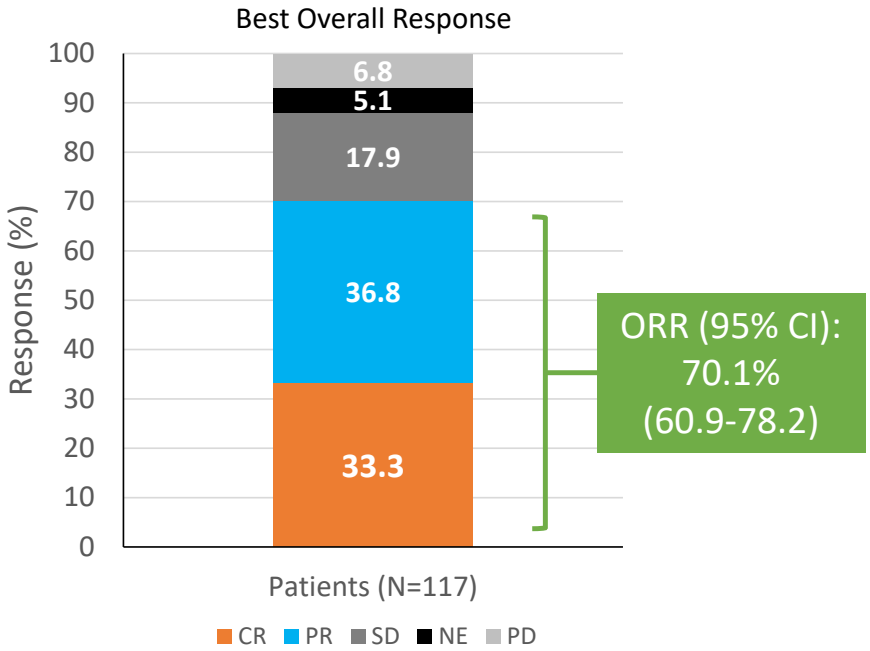
Data cutoff: November 1, 2021

[a] Includes prior HSCT; [b] Missing or not evaluable.

ECOG, Eastern Cooperative Oncology Group; HSCT, hematopoietic stem cell transplant.

1. Cheson BD, et al. *J Clin Oncol*. 2014; 32(27):3059-68.

Efficacy – Overall Response Rate[a]



Best Overall Response in Patients with or without prior SCT

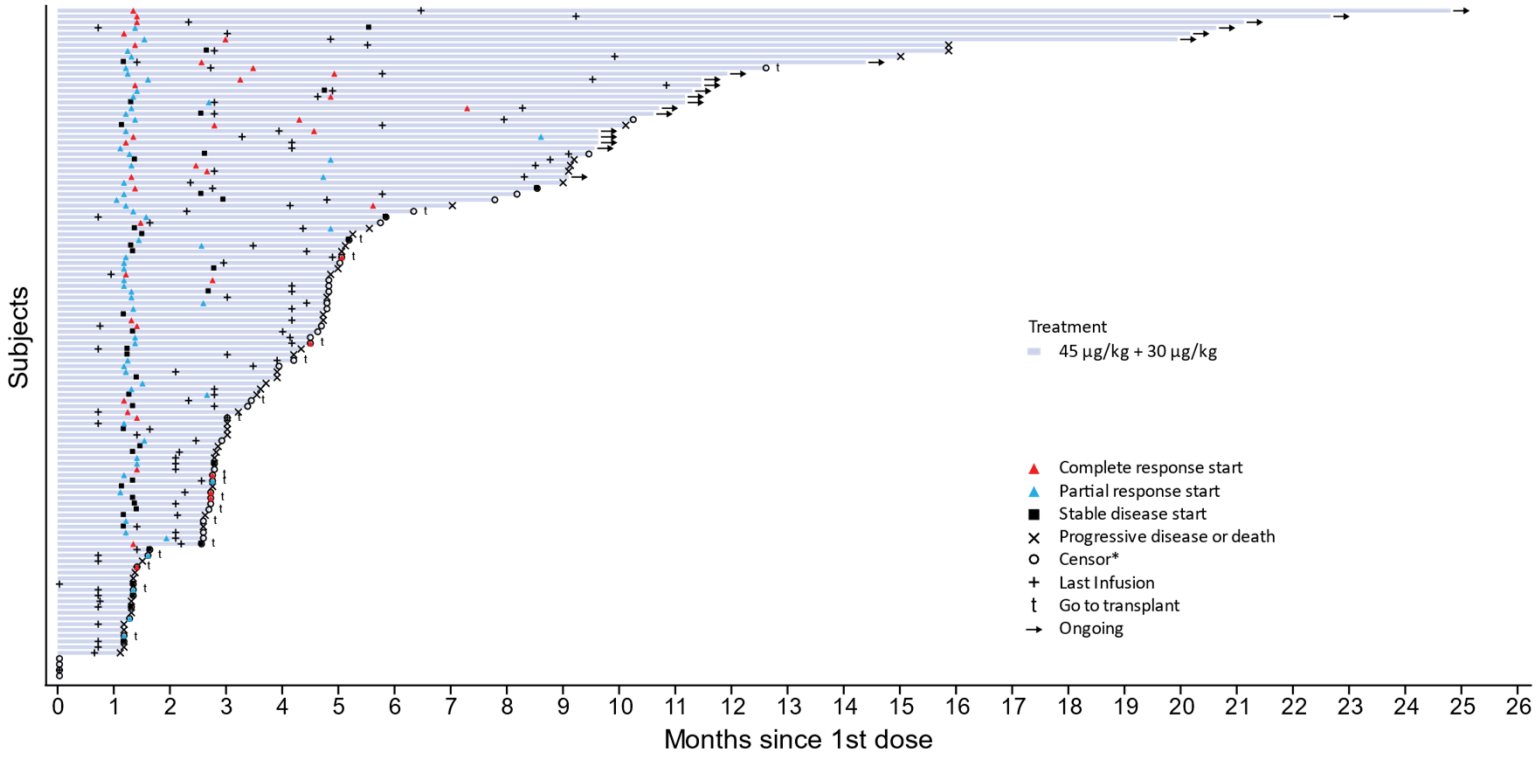
Best Overall response, n (%)[b]	BV and CHPi With Prior SCT (n=73), n (%)	BV and CHPi Without Prior SCT (n=43), n (%)
CR	30 (41.1)	8 (18.6)
PR	24 (32.9)	19 (44.2)
SD	13 (17.8)	8 (18.6)
NE[c]	3 (4.1)	3 (7.0)
PD	3 (4.1)	5 (11.6)
ORR 95% CI for ORR	54 (74.0) 62.4-83.5	27 (62.8) 46.7-77.0

Data cutoff: November 1, 2021

[a] The efficacy analysis set includes all treated patients. [b] One patient did not receive BV due to protocol deviation. [c] In contrast to CR, PR, or PD, a BOR of SD can only be made after a patient is on-study for a minimum of 35 days after the first dose of study drug. Any tumor assessment indicating SD before this time period will be considered as non-evaluable for BOR if no assessment after this time period is available.

BOR, best overall response; BV, brentuximab vedotin; CHPi, checkpoint inhibitor; CR, complete response; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; SCT, stem cell transplant.

A Sizeable Proportion of Patients Experience Long-lasting Treatment Effects



- Total number of cycles dosed, median (min, max)
  - 5 (1, 15)
- Duration of treatment (days), median (min, max)
  - 85 (1, 330)

- Most responses were observed after 2 cycles
- 15 patients who initially had a PR had a subsequent CR
- 14 patients discontinued treatment to receive transplant (of which 12 received transplant)[a]

Data cutoff: November 1, 2021

Each bar represents one patient in the study. Response is determined by independent reviewer. Includes all-treated patient population, defined as those patients who received ≥1 dose of Cami.

*Only for censored patients who discontinued the study due to reasons other than progression, or who went on to a different anticancer treatment other than transplant, or who are ongoing but have no disease assessment yet. [a] Patients who received transplant were censored.

Transplant Outcomes

Patients, n	
Patients who discontinued treatment to move to HSCT	14 (2 did not receive HSCT)[a]
Patients who discontinued treatment for other reasons while in PR/CR and moved to HSCT without intercurrent therapies	4

- Overall, of the 16 patients who received transplant:
  - 12 received allogeneic transplant;
    3 patients progressed 2-5 months after HSCT
  - 4 received autologous transplant;
    1 patient progressed 2 months after HSCT
- 9 patients continue follow-up, 5 withdrew consent, 2 died (causes of death: PD; septic shock)

Relevant post-HSCT AEs (reported post data cut-off date)	Number of events
Allogeneic (NMA conditioning, n=7)	
• Grade 3 malnutrition	1
• Grade 4 eye GVHD	1
Allogeneic (MA conditioning, n=4)	
• Grade 3 hemorrhagic cystitis, Grade 4 myocarditis	1
• Grade 3 diarrhea, febrile neutropenia, pericarditis • Grade 4 leukopenia, pericardial effusion, pericardial tamponade	1
• Grade 4 Klebsiella and Pseudomonas sepsis, Grade 5 septic shock	1
Allogeneic (unknown conditioning, n=1) – no relevant AEs reported	
Autologous (n=4)	
• Grade 3 oral mucositis, atrial fibrillation, febrile neutropenia, AKI	1

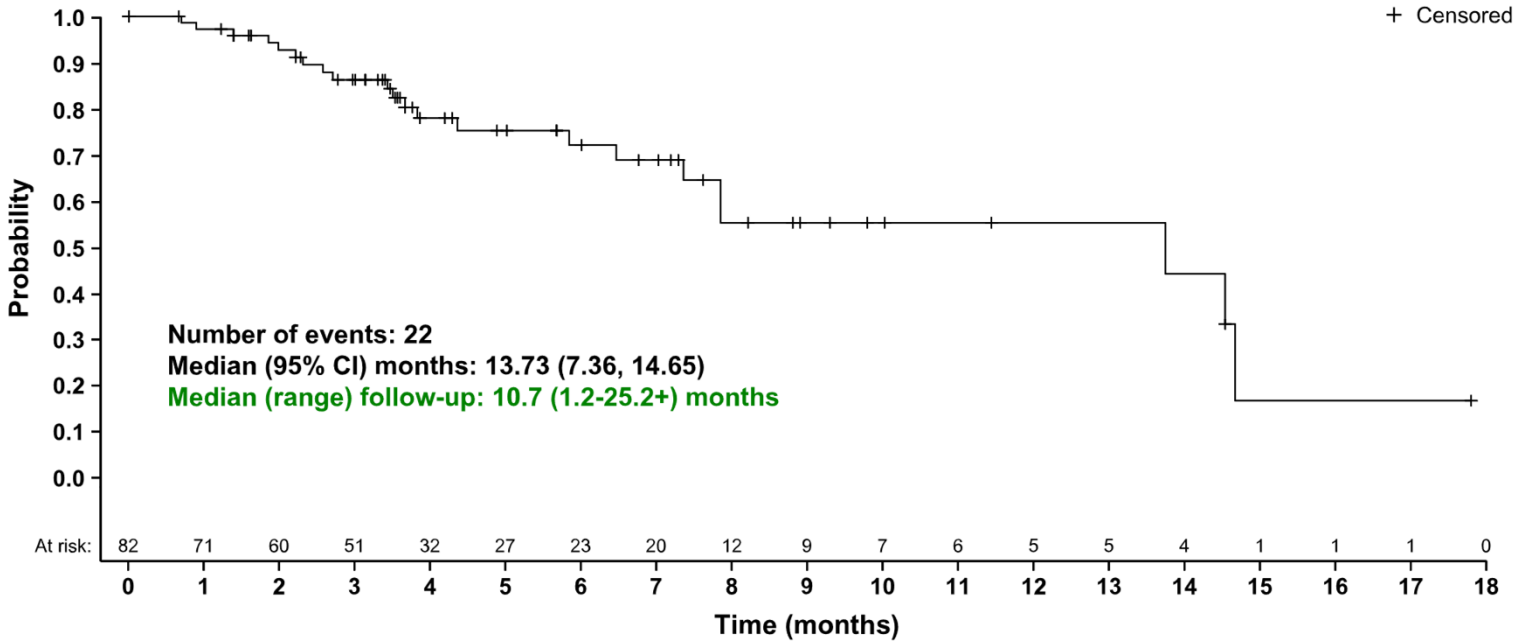
Data cut off: November 1, 2021

[a] Transplant status of 1 patient was unknown at data cutoff and 1 ultimately did not receive transplant.

AE, adverse event; AKI, acute kidney injury; CR, complete response; GVHD, graft versus host disease; HSCT, hematopoietic stem cell transplant; MA, myeloablative; NMA, nonmyeloablative; PD, progressive disease; PR, partial response.

Duration of Response

All-treated Population



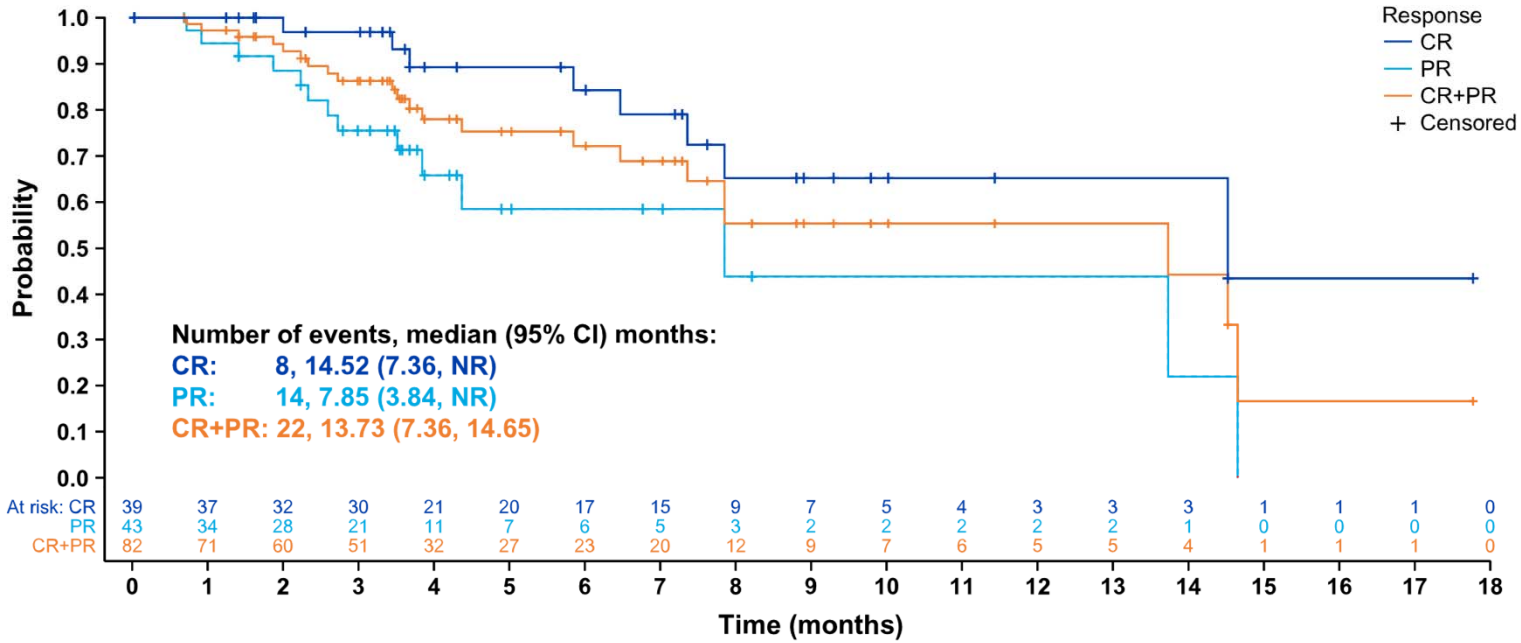
The median time to first CR or PR was 41 days (range 32-148); the median time to first CR was 45 days (range 32-222)

Data cut off: November 1, 2021

CI, confidence interval; CR, complete response; DOR, duration of response; PR, partial response.

Duration of Response

By BOR for Responders



The median time to first CR or PR was 41 days (range 32-148); the median time to first CR was 45 days (range 32-222)

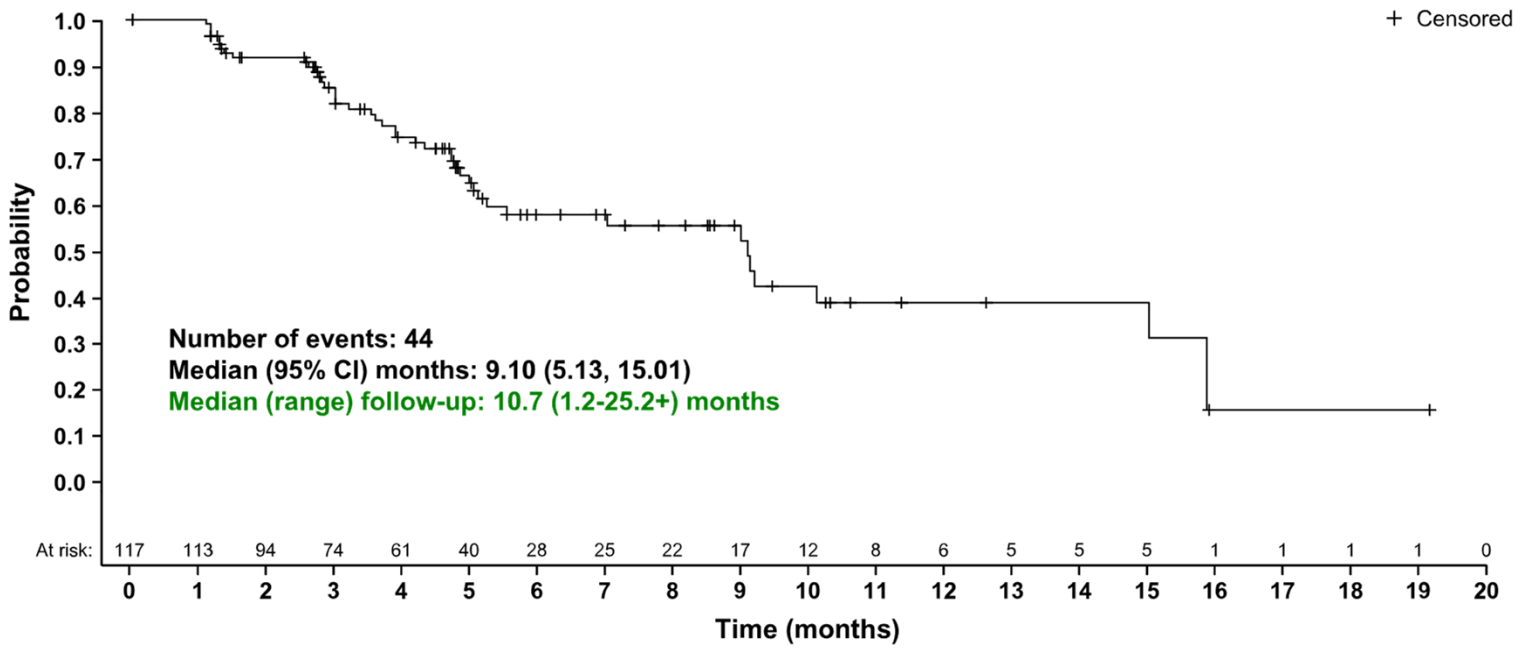
Median (range) follow-up: 10.7 (1.2-25.2+) months

Data cut off: November 1, 2021

BOR, best overall response; CI, confidence interval; CR, complete response; DOR, duration of response; NR, not reached; PR, partial response.

Progression-free Survival by Independent Reviewer

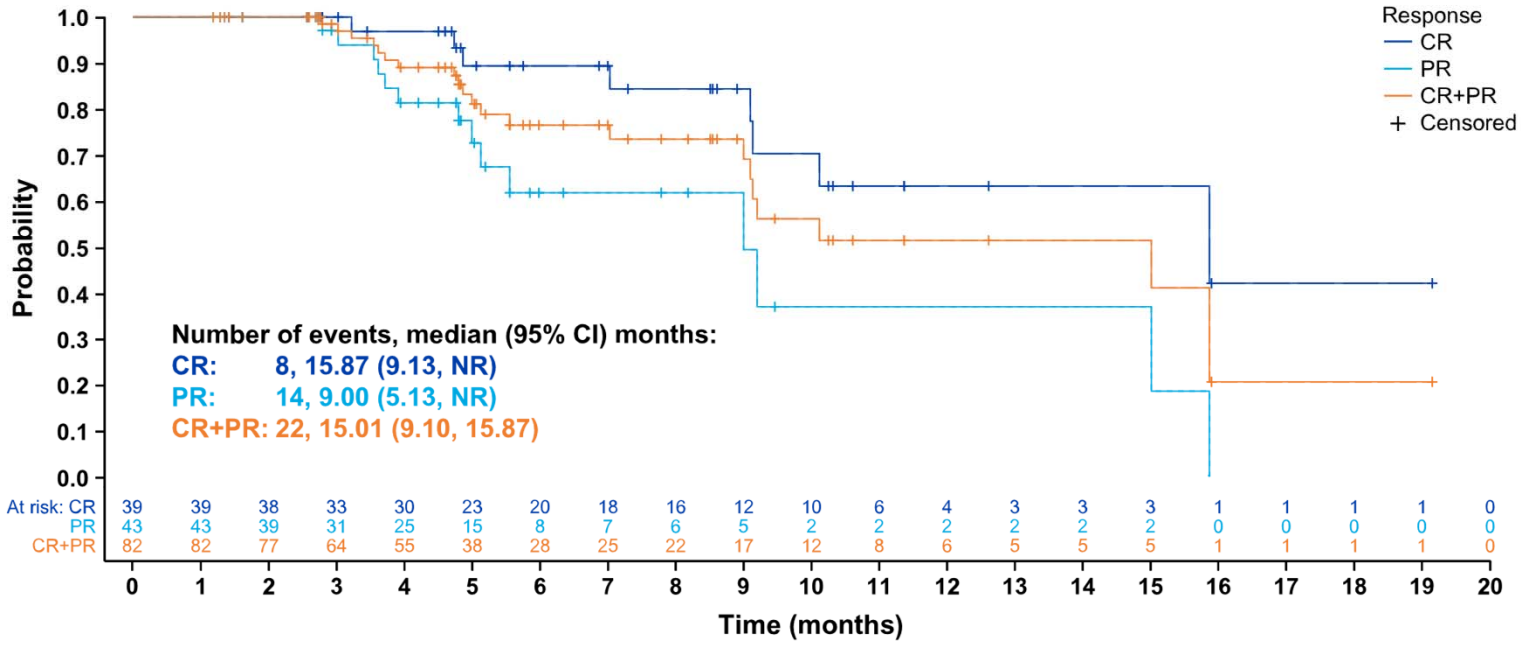
All-treated Population



Data cut off: November 1, 2021
CI, confidence interval.

Progression-free Survival by Independent Reviewer

By BOR for Responders



Median (range) follow-up: 10.7 (1.2-25.2+) months

Data cut off: November 1, 2021

BOR, best overall response; CI, confidence interval; CR, complete response; NR, not reached; PR, partial response.

Safety –TEAEs

All-grade TEAEs in ≥25% of patients, n (%)	Total (N=117)
Any TEAE	116 (99.1)
Fatigue	45 (38.5)
Maculopapular rash	38 (32.5)
Pyrexia	35 (29.9)
Nausea	32 (27.4)
Rash	31 (26.5)
All-grade PBD-related TEAEs	
Skin/nail reactions	87 (74.4)
Hepatobiliary test abnormalities[a]	34 (29.1)
Edema/effusion	20 (17.1)

Grade ≥3 TEAEs in ≥5% of patients, n (%)	
Thrombocytopenia	11 (9.4)
Anemia	10 (8.5)
Hypophosphatemia	9 (7.7)
Neutropenia	9 (7.7)
Maculopapular rash	8 (6.8)
Lymphopenia	6 (5.1)
Grade ≥3 PBD-related TEAEs	
Skin/nail reactions	24 (20.5)
Hepatobiliary test abnormalities[a]	8 (6.8)
Edema/effusion	0 (0)

- TEAEs leading to dose delay/reduction or withdrawal occurred in 66 patients (56.4%) and 32 patients (27.4%), respectively
- Serious TEAEs or fatal TEAEs occurred in 46 patients (39.3%) and 4 patients (3.4%), respectively

Data cut off: November 1, 2021

[a] Includes preferred terms grouped under "liver function test": GGT increased, ALT increased, AST increased, blood alkaline phosphatase increased, hypoalbuminaemia, blood bilirubin increased, ascites, and transaminases increased.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; PBD, pyrrolobenzodiazepine; TEAE, treatment-emergent adverse event.

Safety – Immune-related Adverse Events

- Immune-related TEAEs (ir-TEAEs) occurred in 38 patients (32.5%)
- Grade ≥3 ir-AEs (TEAEs and non-TEAEs) occurred in 10 patients:
  - Median age (range): 45.5 years (22-75)
  - 8/10 patients had prior autologous transplant
  - Median number of Cami cycles (range): 3.5 (2-12)
  - 50% grade ≥3 ir-AEs presented after 2-3 cycles and 50% had onset after 30 days post-last dose
  - Median days since last checkpoint inhibitor (range): 183 (76-2097)

Summary of Grade ≥3 ir-AEs

Patient	Grade ≥3 ir-AEs by Preferred Term	Max grade	Duration (days)	Outcome at last assessment
1	Autoimmune hemolytic anemia	3	5	Recovered
2	Autoimmune hepatitis	4	52	Recovered
3	Bone marrow failure	5	9	Fatal
4	Diabetic ketoacidosis	4	3	Recovered
5	Diabetic ketoacidosis/Type 1 diabetes	4	29	Not recovered[a]
6	Drug-induced liver injury	3	104	Recovered
7	Drug-induced liver injury	3	17	Recovered
8	Lichenoid keratosis	4	175	Not recovered[b]
9	Tubulointerstitial nephritis	3	6	Recovered
10	Tubulointerstitial nephritis	3	130	Recovered

Data cut off: November 1, 2021
[a] Ongoing, decreased to grade 1; [b] Patient died of progressive disease.
PBD, pyrrolobenzodiazepine; TEAE, treatment-emergent adverse event.

Safety – Patients with Guillain–Barré Syndrome (GBS)/polyradiculopathy

- Baseline characteristics:
  - Median age (range): 35 years (23-68)
  - 3/8 patients had prior SCT
  - Median days since last checkpoint inhibitor (range): 187 (50-377)
- Median number of Cami cycles (range): 3.5 (2-7)
  - 4/8 cases presented after 2 cycles; 3/8 had onset after 30 days post last-dose

Summary of Patients with GBS/polyradiculopathy

Patient	AE by preferred term	Max grade	Duration (days)	IVIG/PLEX/ Steroids	Outcome at last assessment
1	GBS	4	523	Y/Y/Y	Ongoing at grade 1
2	GBS	4	43	Y/Y/N	Recovered
3	GBS	3	50	Y/Y/Y	Not recovered; patient died of sepsis
4	GBS	3	287	Y/N/Y	Ongoing at grade 1
5	GBS	3	111	Y/Y/Y	Ongoing at grade 1[a]
6	GBS	2	119	Y/N/N	Recovered
7	Polyneuropathy[b], Meningitis, Facial paralysis, SIADH	4	72	Y/N/Y	Recovered
8	Radiculopathy	2	165	Y/Y/Y	Recovered

Data cut off: November 1, 2021

[a] Also received rituximab with clinical improvement. [b] Verbatim: polyradiculoneuritis.

IVIG, intravenous immunoglobulin; PLEX, plasma exchange; SCT, stem cell transplant; SIADH, syndrome of inappropriate secretion of antidiuretic hormone.

Conclusions

Efficacy

- With median follow-up of 10.7 months, Cami demonstrated an ORR of 70.1% (CR of 33.3%) in heavily pretreated patients with R/R cHL after BV and PD-1 blockade failure
- Median DOR was 13.7 months and median PFS was 9.1 months

Safety

- Safety is consistent with prior findings, including similar incidence rates of GBS/polyradiculopathy
- Immune-related AEs, similar to those observed in patients treated with checkpoint inhibitors, were observed in patients treated with Cami
- GBS/polyradiculopathy remains a concern. With prompt management, such as intravenous immunoglobulin, plasma exchange, and/or high-dose steroids, GBS resolved in 4/8 patients and decreased in severity to grade 1 in 3/8 patients

Data cut off: November 1, 2021

AE, adverse event; BV, brentuximab vedotin; cHL, classical Hodgkin lymphoma; CR, complete response; DoR, duration of response; GBS, Guillain–Barré Syndrome; ORR, overall response rate; PD-1, programmed cell death protein 1; PFS, progression-free survival; R/R, relapsed/refractory.