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)

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INTRODUCTION

- There are limited treatment options available for patients with relapsed/refractory (R/R) cHL who have disease refractory to or that relapses following brentuximab vedotin 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 pyrrolobenzodiazepine (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 overall response rate of 66.3%, with a complete response rate of 27.7% (presented at ICML 2021)[4]

OBJECTIVE

To present updated efficacy and safety data from the phase 2 study (NCT04052997)

STUDY DESIGN

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

45 µg/kg	→	30 µg/kg
Cycles 1 & 2		Cycle 3 onwards, up to 1 year[b]

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

[a]Primary analysis of efficacy and safety in the all-treated population is 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.

METHODS

Key Inclusion and Exclusion Criteria

Inclusion Criteria

- Male or female
- ≥18 years (≥16 years in the 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 the start of Cami treatment
- History of neuropathy considered of autoimmune origin (eg, polyradiculopathy, including GBS and myasthenia gravis) or other CNS autoimmune diseases, such as poliomyelitis or MS
- Recent infection (<4 weeks of cycle 1, day 1) that was considered caused by prespecified pathogens
- HIV, HBV, or HCV infection needing antiviral therapy/prophylaxis
- Clinically significant third-space fluid accumulation (ie, 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.

RESULTS

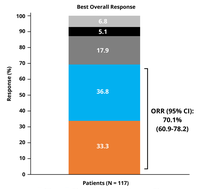
Table 1: Baseline characteristics

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)[a], 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.

Figure 1. Efficacy—overall response rate[a]

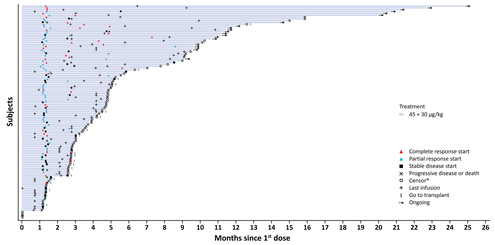


Data cutoff: November 1, 2021
[a]The efficacy analysis set includes all treated patients. [b]One patient did not receive BV due to protocol deviation. [c]In contrast to CR, PR, or PD, a BOR of SD can only be made after a patient is on study for a minimum of 35 days after the first dose of the study drug. 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.

Table 2. Best overall response in patients with or without prior SCT

Best overall response, n (%)[a]	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[b]	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

Figure 2. 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 partial response had a subsequent complete response
- 14 patients discontinued treatment to receive a transplant (of which 12 received transplants)[a]

Data cutoff: November 1, 2021
Each bar represents one patient in the study. The response is determined by an 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, who went on to a different anticancer treatment other than a transplant, or who are ongoing but have no disease assessment yet. [a]Patients who received transplant were censored.

Tables 3 and 4: Transplant outcomes

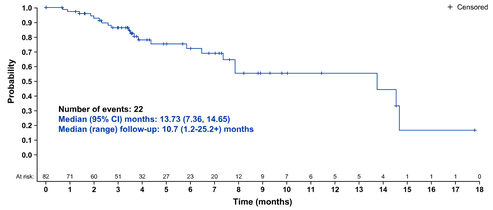
	Patients, n
Patients who discontinued treatment to move to HSCT	12 (2 did not receive HSCT)[a]
Patients who discontinued treatment for other reasons while in PR/CR and moved to HSCT without intercurrent therapies	4

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

Data cutoff: 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; NA, myeloablative; NMA, nonmyeloablative; PD, progressive disease; PR, partial response.

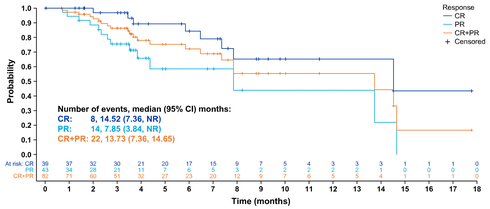
Relevant post-HSCT AEs (reported post data cutoff date)	Number of events
Allogeneic (NMA conditioning, n = 7)	
Grade 3 malnutrition	1
Grade 4 eye GVHD	1
Allogeneic (MA conditioning, n = 4)	
Grade 3 hemorrhagic cystitis, grade 4 myocarditis	1
Grade 3 diarrhea, febrile neutropenia, pericarditis	1
Grade 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

Figure 3: Duration of response—all-treated population



Data cutoff: November 1, 2021
CR, complete response; DOR, duration of response; PR, partial response.

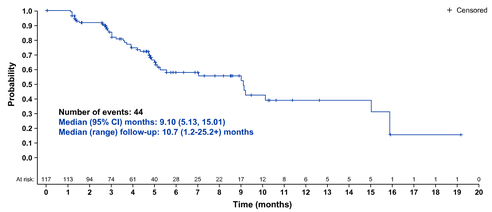
Figure 4: Duration of response—all-treated population



Data cutoff: November 1, 2021
BOR, best overall response; CR, complete response; NR, not reached; PR, partial response.

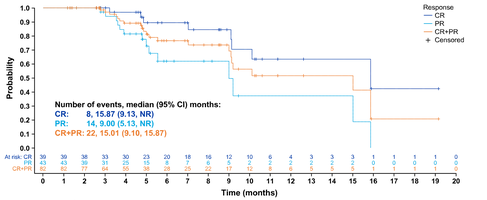
- The median time to first CR or PR was 41 days (range 32-148); the median time to first CR was 45 days (range 32-222)
- Median (range) follow-up: 10.7 (1.2-25.2+) months

Figure 5: Progression-free survival by independent reviewer—all-treated population



Data cutoff: November 1, 2021

Figure 6: Progression-free survival by independent reviewer—by BOR for responders



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

Data cutoff: November 1, 2021
BOR, best overall response; CR, complete response; NR, not reached; PR, partial response.

Table 5: 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)

Grade ≥3 TEAEs in ≥5% of patients, n (%)	Total (N = 117)
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)

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 PBD-related TEAEs	
Skin/nail reactions	24 (20.5)
Hepatobiliary test abnormalities[a]	8 (6.8)
Edema/effusion	0 (0)

- TEAEs leading to a 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 cutoff: November 1, 2021
[a]Includes preferred terms grouped under 'liver function test': GGT increased, ALT increased, AST increased, blood alkaline phosphatase increased, hypoalbuminemia, blood bilirubin increased, ascites, and transaminases increased.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; PBD, pyrrolobenzodiazepine; TEAE, treatment-emergent adverse event.

Table 6: Safety—immune-related adverse events

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[a]
9	Tubulointerstitial nephritis	3	6	Recovered
10	Tubulointerstitial nephritis	3	130	Recovered

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

- 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 after the last dose
  - Median days since the last checkpoint inhibitor (range): 183 (76-2097)

Table 7: Safety—patients with Guillain–Barré Syndrome (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

[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

- 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 after the last dose

CONCLUSIONS

Efficacy

- With a 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
- The median DOR was 13.7 months, and the 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
- 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

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