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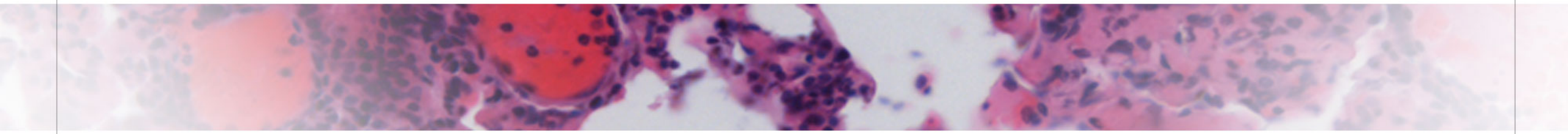

# Preliminary Results of a Phase 2 Study of Camidanlumab Tesirine (Cami), a Novel Pyrrolobenzodiazepine-Based Antibody-Drug Conjugate, in Patients With Relapsed or Refractory Hodgkin Lymphoma

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# Introduction

- Patients with R/R cHL who have no response to treatments such as brentuximab vedotin (BV) and PD-1 blockade, or initial response followed by progressive disease, have limited therapeutic options[1–10]
  - Novel treatments are needed to address this significant unmet need

- Camidanlumab tesirine (Cami) is an antibody-drug conjugate previously evaluated for safety and efficacy in R/R cHL in a Phase 1 study
  - Generally acceptable safety profile and high response rates were demonstrated[10]

- Here, we present efficacy and safety data from a Phase 2 trial of single-agent Cami in patients with R/R cHL; this preliminary analysis was conducted after meeting a protocol-specified criterion[a] for pausing enrollment

[a]≥2 cases of Guillain–Barré syndrome or other relevant severe neurologic toxicity.

1. Mehta-Shah N, et al. *Blood* 2018;131:1698–703; 2. Mottok A, et al. *Blood* 2018;131:1654–65; 3. Fields PA, et al. *Medicine* 2017;45:305–10; 4. Glimelius I, et al. *J Intern Med* 2017;281:247–60; 5. Eichenauer DA, et al. *Ann Oncol* 2018;29:iv19–29; 6. Shanbhag S, et al. *CA Cancer J Clin* 2018;68:116–32; 7. Marchi E, et al. *CA Cancer J Clin* 2020;70:47–70; 8. Crump et al. *Blood* 2017;130:1800–08; 9. Miller M, et al. *CA Cancer J Clin* 2019;69:363–85; 10. Collins G, et al. Abstract 055, ICML, Lugano, Switzerland, Jun 18–22, 2019.

**cHL**, classical Hodgkin lymphoma; **PD-1**, programmed cell death protein 1; **R/R**, relapsed or refractory.

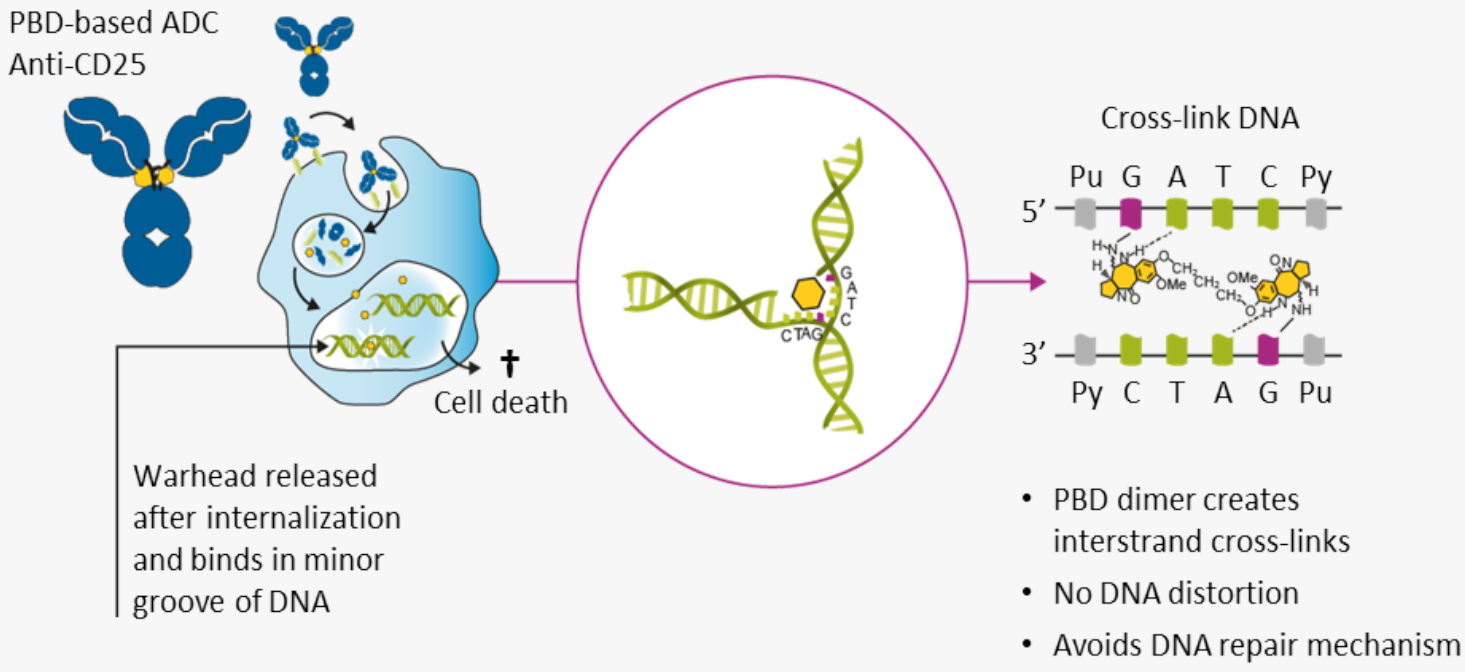
# Composition and Mechanism of Action

## Cami composition

- Human IgG1 anti-CD25 mAb stochastically conjugated to PBD dimer warhead

## Mechanism of action[1–3]

- Death of CD25-expressing tumor cells
- Depletion of CD25-expressing T cells in HL tumor microenvironment
- Possible bystander killing of CD25-negative cells




1. Hartley JA. *Expert Opin Investig Drugs* 2011;20:733–44; 2. Flynn MJ, et al. *Mol Cancer Ther* 2016;15:2709–21; 3. Zammarchi F, et al. *J ImmunoTher Cancer* 2020;8:e000860.
**ADC**, antibody-drug conjugate; **IgG**, immunoglobulin G; **mAb**, monoclonal antibody; **PBD**, pyrrolobenzodiazepine.

# Study Methods

## Study design

- Single-arm, multicenter, open-label, Phase 2 trial (NCT04052997)

## Primary objective

- Efficacy of single-agent Cami by ORR[a]

## Secondary objectives

- DoR, CRR, RFS, PFS, OS, and % patients receiving HSCT
- Safety

## Key inclusion criteria

- R/R cHL
- Aged ≥16 years (USA), ≥18 years (outside USA)
- ≥3 prior lines of treatment (≥2 lines if HSCT-ineligible)
  - Including brentuximab vedotin and PD-1 blockade
- ECOG performance status 0–2

## 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]**

[a]Per Lugano classification, determined by central review; [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.

**CRR**, complete response rate; **DoR**, duration of response; **ECOG**, Eastern Cooperative Oncology Group; **HSCT**, hematopoietic stem cell transplantation; **IV**, intravenous; **ORR**, overall response rate; **OS**, overall survival; **PFS**, progression-free survival; **RFS,** relapse-free survival.

# Patient Characteristics

No. of patients enrolled and treated with Cami at data cut-off

**51**

Median (range) No. of Cami cycles

**5 (1–11)**

No. of patients previously treated with BV and PD-1 blockade[a]

**50 (98.0%)**

| Characteristic | Total (n=51) |
|---|---|
| **Sex, n (%)** | |
| Male | 36 (70.6) |
| Female | 15 (29.4) |
| **Age, years, median (min, max)** | 36 (20–74) |
| **Histology** | |
| Nodular sclerosis cHL | 40 (78.4) |
| Other/unknown/not evaluable[b] | 11 (21.6) |
| **ECOG status, n (%)** | |
| 0 | 29 (56.9) |
| 1 | 19 (37.3) |
| 2 | 3 (5.9) |
| **No. prior systemic therapies[c], median (min, max)** | 7 (3–20) |
| **Disease status after first-line therapy, n (%)** | |
| Relapsed[d] | 35 (68.6) |
| Refractory[e] | 12 (23.5) |
| Other[f] | 4 (7.8) |
| **Refractory to last systemic therapy, n (%)** | 25 (49.0) |
| **Prior HSCT, n (%)** | 37 (72.5) |
| Autologous[g] | 31 (60.8) |
| Allogeneic | 2 (3.9) |
| Both | 4 (7.8) |

[a]One patient (1/51; 2%) had a protocol deviation of no prior treatment with BV; [b]Includes mixed cellularity and lymphocyte-rich cHL, and subtype not specified/unknown; [c]Includes prior HSCT; [d]Complete or partial response followed by relapse; [e]Stable or progressive disease; [f]Missing or not evaluable; [g]Includes 1 patient with tandem autologous HSCT. Safety analysis set (n=51). Data cut-off: August 24, 2020.

# Efficacy – Overall Response Rate

**ORR (CR+PR)**

**83.0% (39/47)**

**95% CI: 69.2, 92.4**

No. of patients with CR

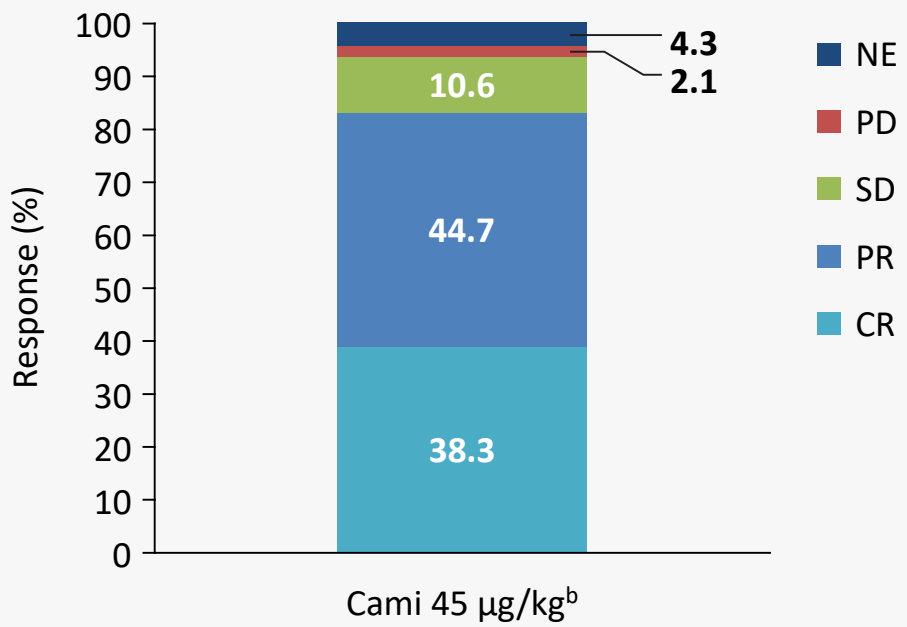
**18 (38.3%)**

No. of patients with PR

**21 (44.7%)**

No. of patients who went on to consolidation with HSCT[a]

**5 (10.6%)**




[a]One further patient had HSCT planned but not confirmed by data cut-off. 4/5 patients received autologous and 1 patient received allogeneic HSCT; [b]45 µg/kg for 2 cycles, then 30 µg/kg for subsequent cycles. Response assessment per Lugano classification as determined by central review. Efficacy analysis set (n=47); includes patients who started treatment ≥6 weeks before data cut-off with valid post-baseline disease assessment results from independent review or death prior to first scheduled disease assessment per protocol. Data cut-off: August 24, 2020.

**CI,** confidence interval; **CR**, complete response; **NE**, not evaluable; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease.

# Safety – TEAEs (1/2)

| Most common TEAEs (≥20% of patients)[a] | |
|---|---|
| **Fatigue** | 26 (51.0) |
| **Pyrexia** | 20 (39.2) |
| **Nausea** | 19 (37.3) |
| **Maculopapular rash** | 18 (35.3) |
| **Headache** | 14 (27.5) |
| **Pruritus** | 14 (27.5) |
| **Anemia** | 13 (25.5) |
| **Arthralgia** | 12 (23.5) |
| **Diarrhea** | 11 (21.6) |
| **Gamma-glutamyltransferase increased** | 11 (21.6) |
| **Rash** | 11 (21.6) |

| Most common Grade ≥3 TEAEs (≥5% of patients)[a] | |
|---|---|
| **Hypophosphatemia** | 6 (11.8) |
| **Gamma-glutamyltransferase increased** | 5 (9.8) |
| **Alanine aminotransferase increased** | 3 (5.9) |
| **Maculopapular rash** | 3 (5.9) |

No. of patients who experienced TEAEs
**49 (96.1%)**

No. of patients with Grade ≥3 TEAEs
**32 (62.7%)**

TEAEs leading to dose reduction/delay
**6 (11.8%)**

TEAEs leading to treatment withdrawal
**7 (13.7%)**

[a]Preferred term. Safety analysis set (n=51). Data cut-off: August 24, 2020. Data shown as n (%).

**TEAE**, treatment-emergent adverse event, defined as AE occurring or worsening from time of first dose to either 30 days post last dose or start of new anticancer therapy/procedure, whichever occurred first.

# Safety – TEAEs (2/2)

## TEAEs thought to be PBD-associated included:

**Skin reactions and nail disorders**

- All grades: **37 (72.5%)**
- Grade ≥3: **9 (17.6%)**

**Liver function test abnormalities**

- All grades: **17 (33.3%)**
- Grade ≥3: **6 (11.8%)**

**Edema or effusion**

- All grades: **9 (17.6%)**
- Grade ≥3: **0 (0%)**

## Fatal TEAEs

**Two fatal TEAEs (3.9% of patients):**

- Myocardial infarction
  - Considered not related to treatment
- Respiratory failure
  - Considered unlikely related to treatment

Safety analysis set (n=51). Data cut-off: August 24, 2020.

# Safety – Study Pause

- Enrollment pause due to meeting protocol-specified criterion:
  - ≥2 cases of Guillain–Barré syndrome (GBS) or other relevant severe neurologic toxicity
- Assessment by independent review
- No. of cases of GBS/polyradiculopathy: **3 (6.4%)**
  - Grade 4 GBS (inflammatory demyelinating polyneuropathy[a])
  - Grade 2 radiculopathy (radiculitis[a])
  - Grade 2 GBS
- Following review of safety and efficacy data, enrollment pause lifted

[a]Verbatim term. Safety analysis set (n=51). Data cut-off: August 24, 2020.

# Conclusions

**Encouraging antitumor activity in patients with R/R cHL receiving single-agent treatment with Cami**

- Patients were heavily pre-treated and **98.0%** had received prior BV and PD-1 blockade
- ORR (CR+PR) to treatment was high at **83.0%**, and **38.3%** of patients had CR

**Five (10.6%) patients went on to consolidation with HSCT**

**Safety in this Phase 2 preliminary analysis consistent with Phase 1 study**

- No new safety signals identified
- Similar incidence of GBS/polyradiculopathy

**Enrollment pause lifted after review of safety and efficacy data**

- Study enrollment continues

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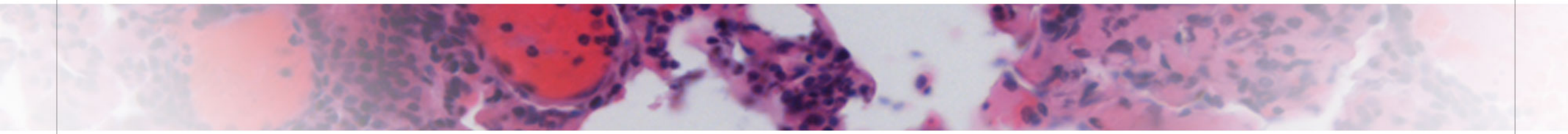

# Thank you for listening

Questions are welcome