Exploratory Analysis of Factors Influencing Eficacy and Safety of Camidanlumab Tesirine: Data from the Open-Label, Multicenter, Phase 2 Study of Patients with Relapsed or Refractory Classical Hodgkin Lymphoma (R/R cHL)

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Introduction: Despite most patients with cHL being cured with standard therapies, a proportion of patients are refractory or relapse after first- and second-line treatments (1L/2L), including stem cell transplantation, and there are limited treatment options available after failure of brentuximab vedotin (BV) and PD-1 blockade. Camidanlumab tesirine (Cami) is an antibody-drug conjugate comprising an anti-CD25 monoclonal antibody conjugated through a cleavable linker to a pyrrolobenzodiazepine (PBD) dimer. Cami has shown notable single-agent anti-tumor activity and manageable toxicity in the Phase 2 trial of patients with R/R cHL (Carlo-Stella et al, *Hemasphere* 2022;6:102-103).

Objectives: To assess the clinical response and safety of Cami by subgroups based on demographics, known risk factors impacting outcomes in patients

with R/R cHL, and factors with potential relevance to Cami's mechanism of action.

Methods: This analysis was based on the open-label, multicenter, Phase 2 study of Cami monotherapy in patients with R/R cHL after ≥3 prior lines of therapy (NCT04052997). Cami was administered (30-minute infusion) on day 1 of each 3-week cycle at 45 µg/kg for 2 cycles, then 30 µg/kg for subsequent cycles. Subgroup analyses (data cutoff: March 16, 2022) were conducted (Table 1). Effcacy outcomes included the overall response rate (ORR) and median duration of response (mDOR); statistical significance was assessed by comparison of 95% confidence intervals. Safety was assessed by incidence of treatment emergent adverse events (TEAEs).

Results: There were no significant differences in effcacy outcomes between demographic subgroups based on age or sex (Table 1). The ORR was similar for patients who were refractory or relapsed after 1L therapy (72.4% vs 72.2%). Despite the higher number of patients who were refractory after last line therapy versus those who relapsed, the ORR was not significantly different between the two groups (68.2% vs 78.4%). The response to Cami did not depend on the prior response to PD-1 inhibition or the time since the last PD-1 inhibitor use. The ORR was similar for patients who were refractory to PD-1 inhibition or relapsed (66.2% vs 75.8%) and for patients who were treated with Cami ≤4 months and >4 months since the last PD-1 inhibitor (69.0% vs 71.7%).

No statistically significant differences in the ORR were observed based on the number of prior lines of therapy, prior HSCT, or region. However, the complete response rate (CRR) for patients who received prior HSCT was 41.9% vs 18.6% in patients without HSCT; the mDOR was 13.73 months in patients with prior HSCT vs 5.85 in patients without prior HSCT. Median DOR was similar between North American (NA) and European (EU) patients (13.77 months vs 13.73 months). However, NA patients had improved CRR vs EU patients (44.6% vs 23%), and differences were more pronounced in NA vs EU patients with prior HSCT (52.4% vs 28.1%).

Cami's tolerability was similar across most subgroups. The safety profile of Cami was similar in older compared with younger patients, as indicated by similar incidences of TEAEs overall, grade ≥3 TEAEs, and groupings by system organ class. The incidence of any grade TEAEs was similar between NA and EU patients (100% vs 98.4%). Patients with prior HSCT had more grade ≥3 TEAEs vs those without prior HSCT (73% vs 58.1%).

Conclusions: Evidence from preliminary subgroup analyses suggests that response to Cami was independent of age, sex, and response to and timing

of last PD-1 inhibitor. Differences in Cami's safety and effcacy were noted by prior transplant and region. Although a difference in CRR was observed between NA and EU, this did not result in a difference in mDOR or ORR between the two regions. These preliminary analyses should be interpreted with caution as subgroups were small and limited in statistical comparison. Exploratory analyses to identify predictive markers of GBS/polyradiculopathy observed in Cami trials are ongoing and results will be also presented. These results suggest that Cami shows antitumor activity across patient subgroups, including heavily pretreated and older patients.

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Table 1: Subgroups and Corresponding Overall Response Rates

Subgroup	Complete response (CR) rate (95% CI)	Overall response rate (CR+PR) (95% CI)	Patients, n
Region			
North America	44.6 (31.3, 58.5)	75.0 (61.6, 85.6)	56
Europe	23.0 (13.2, 35.5)	65.6 (52.3, 77.3)	61
Age			
<50 years	34.1 (24.0, 45.4)	70.7 (59.6, 80.3)	82
≥50 years	31.4 (16.9, 49.3)	68.6 (50.7, 83.1)	35
Sex			
Female	29.5 (16.8, 45.2)	79.5 (64.7, 90.2)	44
Male	35.6 (24.7, 47.7)	64.4 (52.3, 75.3)	73
Disease stage			
I-II	28.0 (12.1, 49.4)	84.0 (63.9, 95.5)	25
III-IV	35.2 (25.4, 45.9)	67.0 (56.4, 76.5)	91
Extranodal involvement			
Yes	33.3 (20.8, 47.9)	68.6 (54.1, 80.9)	51
No	33.3 (22.2, 46.0)	71.2 (58.7, 81.7)	66
Number of prior systemic therapies			
≤5 lines	23.9 (12.6, 38.8)	69.6 (54.2, 82.3)	46
6-7 lines	41.9 (24.5, 60.9)	67.7 (48.6, 83.3)	31
≥8 lines	37.5 (22.7, 54.2)	72.5 (56.1, 85.4)	40
Response to first-line systemic therapies			
Refractory	34.5 (17.9, 54.3)	72.4 (52.8, 87.3)	29
Relapse	32.9 (22.7, 44.4)	72.2 (60.9, 81.7)	79
Response to last-line systemic therapies			
Refractory	33.3 (22.2, 46.0)	68.2 (55.6, 79.1)	66
Relapse	37.8 (22.5, 55.2)	78.4 (61.8, 90.2)	37
Prior HSCT			
Yes	41.9 (30.5, 53.9)	74.3 (62.8, 83.8)	74
No	18.6 (8.4, 33.4)	62.8 (46.7, 77.0)	43
Region by prior HSCT			
North America w/ HSCT	52.4 (36.4, 68.0)	76.2 (60.5, 87.9)	42
North America w/o HSCT	21.4 (4.7, 50.8)	71.4 (41.9, 91.6)	14
Europe w/ HSCT	28.1 (13.7, 46.7)	71.9 (53.3, 86.3)	32
Europe w/o HSCT	17.2 (5.8, 35.8)	58.6 (38.9, 76.5)	29
Response to last PD-1 inhibitor			
Refractory	32.4 (21.8, 44.5)	66.2 (54.0, 77.0)	71
Relapse	36.4 (20.4, 54.9)	75.8 (57.7, 88.9)	33
Time from last PD-1 inhibitor			
≤4 months	32.8 (21.0, 46.3)	69.0 (55.5, 80.5)	58
>4 months	32.1 (19.9, 46.3)	71.7 (57.7, 83.2)	53