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ORAL ABSTRACTS

624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Efficacy and Safety of Valemetostat Monotherapy in Patients with Relapsed or Refractory Peripheral T-Cell Lymphomas: Primary Results of the Phase 2 VALENTINE-PTCL01 Study

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Introduction: Peripheral T-cell lymphoma (PTCL) is an aggressive non-Hodgkin lymphoma (NHL), with limited available treatment options for patients (pts) with relapsed or refractory (R/R) disease. Valemetostat tosylate (valemetostat) is a novel and potent dual inhibitor of enhancer of zeste homolog (EZH)2 and EZH1, which is approved in Japan for the treatment of R/R adult T-cell leukemia/lymphoma (ATLL). Here, we report primary results for pts with R/R PTCL treated with valemetostat in the open-label, single-arm, global, phase 2 VALENTINE-PTCL01 study (DS3201-A-U202; NCT04703192).
Methods: Pts were ≥ 18 years of age, had a confirmed diagnosis of PTCL, had R/R disease after ≥ 1 prior line of systemic therapy, and pts with anaplastic large cell lymphoma (ALCL) had received prior brentuximab vedotin treatment. Pts received oral valemetostat 200 mg/day in continuous 28-day cycles until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR), assessed by blinded independent central review of PTCL following computed tomography (CT)-based response assessment according to Lugano 2014 criteria. Secondary efficacy endpoints included duration of response (DOR), progression-free survival (PFS), and overall survival (OS). Positron emission tomography (PET)-CT-based response assessment by Lugano 2014 criteria was an exploratory endpoint. Efficacy analyses included all pts who received ≥ 1 dose of valemetostat and had an eligible PTCL subtype confirmed by central hematopathology review; safety analyses included all pts who received ≥ 1 dose of valemetostat.
Results: A total of 133 pts with R/R PTCL were enrolled and received ≥ 1 dose of valemetostat. Pts had a median age of 69 years (range 22-85) and 91 pts (68.4%) were male. Pts had received a median of 2 prior lines of therapy (range 1-12) and 35 pts (26.3%) received prior hematopoietic cell transplant (HCT; autologous, n = 32; allogeneic, n = 5). PTCL subtype eligibility

was confirmed in 119 pts: 42 pts (31.6%) had angioimmunoblastic T-cell lymphoma (AITL), 41 (30.8%) had PTCL, not otherwise specified (PTCL, NOS), 9 (6.8%) had ALCL (7 [5.3%] *ALK*-negative and 2 [1.5%] *ALK*-positive), 8 (6.0%) had nodal PTCL with T follicular helper cell phenotype, and 19 (14.3%) had other PTCL subtypes.

As of data cutoff (May 5, 2023), 32 pts (24.1%) were still receiving treatment; reasons for treatment discontinuation included progressive or relapsed disease in 46 pts (34.6%), clinical progression in 19 pts (14.3%), adverse event in 13 pts (9.8%), and 12 pts (9.0%) discontinued study drug to proceed with allogeneic HCT. Median treatment duration was 18 weeks (range 0.3-93.4) and median duration of follow-up was 10.5 months (range 0.2-21.5).

Among 119 efficacy-evaluable pts, the CT-based ORR was 43.7% (n = 52) (95% confidence interval [CI], 34.6-53.1), including 17 pts (14.3%) achieving CR and 35 pts (29.4%) achieving PR as best overall response. Median DOR was 11.9 months (95% CI, 7.8-not evaluable [NE]) and median time to response was 8.1 weeks (range 5-37). ORR by PTCL subtype ranged from 31.7% for PTCL, NOS to 54.8% for AITL (Table 1). Using PET-CT-based response assessment, ORR was 52.1% (n = 62) (95% CI, 42.8-61.3), including 32 pts (26.9%) with a complete metabolic response. Median CT-based PFS was 5.5 months (95% CI, 3.5-8.3) and median OS was 17.0 months (95% CI, 13.5-NE).

Of 133 pts in the safety analysis set, 128 pts (96.2%) experienced ≥ 1 treatment-emergent adverse event (TEAE) of any grade, 77 pts (57.9%) experienced grade ≥ 3 TEAEs, and 53 pts (39.8%) experienced serious adverse events. The most common all grade and grade ≥ 3 TEAE was thrombocytopenia (Table 2). Overall, 13 pts (9.8%) experienced a TEAE that led to treatment discontinuation, 21 pts (15.8%) had a TEAE that led to dose reduction, and 66 pts (49.6%) had a TEAE that led to dose interruption.

Conclusions: Valemetostat demonstrated a high ORR of 43.7% with durable responses (median DOR of 11.9 months) in pts with R/R PTCL, and responses were observed across all PTCL subtypes. A valemetostat dose of 200 mg/day was tolerable; safety analysis showed that the most common TEAEs were cytopenias. These primary results from the VALENTINE-PTCL01 study suggest that valemetostat provides a clinically meaningful benefit for pts with R/R PTCL.

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Table 1. Efficacy results per CT-based blinded independent central review assessment by PTCL subtype

Response	AITL (n = 42)	PTCL, NOS (n = 41)	PTCL TFH (n = 8)	ALCL (*ALK*-positive or *ALK*-negative) (n = 9)	Other[a] (n = 19)	All (N = 119)
ORR (CR or PR), n (%)	23 (54.8)	13 (31.7)	4 (50)	3 (33.3)	9 (47.4)	52 (43.7)
95% CI[b]	38.7–70.2	18.1–48.1	15.7–84.3	7.5–70.1	24.4–71.1	34.6–53.1
CR, n (%)	8 (19.0)	4 (9.8)	1 (12.5)	1 (11.1)	3 (15.8)	17 (14.3)
95% CI[b]	8.6–34.1	2.7–23.1	0.3–52.7	0.3–48.2	3.4–39.6	8.5–21.9
PR, n (%)	15 (35.7)	9 (22.0)	3 (37.5)	2 (22.2)	6 (31.6)	35 (29.4)
95% CI[b]	21.6–52.0	10.6–37.6	8.5–75.5	2.8–60.0	12.6–56.6	21.4–38.5
DOR[c], median (range), months	11.9 (1.6–14.9+)	7.9 (0+–14.9+)	NE (5.1–11.1+)	3.8 (3.7–12.0+)	9.2 (3.7–9.5+)	11.9 (0+–14.9+)
95% CI[d]	10.8–NE	3.7–NE	5.1–NE	3.7–NE	3.7–NE	7.8–NE
DOCR[e], median (range), months	NE (0+–12.0+)	11.2 (2.7+–11.2)	5.1 (5.1–5.1)	NE (8.3+–8.3+)	NE (6.5+–9.5+)	11.2 (0+–12.0+)
95% CI[d]	1.7–NE	4.2–NE	NE–NE	NE–NE	NE–NE	4.2–NE

[a]Includes 3 pts with follicular T-cell lymphoma, 1 with primary cutaneous γδ T-cell lymphoma, 1 with primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma, 1 with monomorphic epitheliotropic intestinal T-cell lymphoma, and 13 with other eligible, but undetermined, PTCL subtypes; [b]CI for proportions were computed using the Clopper-Pearson exact method; [c]Duration of response was calculated as the time from first documented response (either CR or PR) to the date of documented disease progression (progressive or relapsed disease) per blinded independent central review assessment or to death due to any cause, whichever occurred first; [d]CI for medians was computed using the Brookmeyer–Crowley method; [e]Duration of CR was calculated as the time from first documented CR to the date of documented disease progression (progressive or relapsed disease) per blinded independent central review assessment or to death due to any cause, whichever occurred first.

AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large cell lymphoma; *ALK*, anaplastic lymphoma kinase; CD8+, cluster of differentiation 8+; CI, confidence interval; CR, complete response; CT, computed tomography; DOCR, duration of CR; DOR, duration of response; NE, not evaluable; ORR, objective response rate; PR, partial response; pt(s), patient(s); PTCL, peripheral T-cell lymphoma; PTCL, NOS, PTCL, not otherwise specified; PTCL TFH, PTCL with T follicular helper cell phenotype.

Table 2. TEAEs in ≥ 10% of patients with R/R PTCL

	R/R PTCL (N = 133)	
	Any grade	Grade ≥ 3
Preferred term	n (%)	
Pts with ≥ 1 TEAE	**128 (96.2)**	**77 (57.9)[a]**
Thrombocytopenia[b]	66 (49.6)	31 (23.3)
Anemia[c]	47 (35.3)	25 (18.8)
Diarrhoea	39 (29.3)	5 (3.8)
Dysgeusia	38 (28.6)	0
Neutropenia[d]	35 (26.3)	23 (17.3)
COVID-19	28 (21.1)	4 (3.0)
Nausea	23 (17.3)	1 (0.8)
Cough	20 (15.0)	0
Pyrexia	20 (15.0)	0
Decreased appetite	19 (14.3)	2 (1.5)
Fatigue	19 (14.3)	2 (1.5)
Asthenia	17 (12.8)	4 (3.0)
Oedema peripheral	16 (12.0)	1 (0.8)
Pruritus	16 (12.0)	0
Alopecia	14 (10.5)	0
AST increased	14 (10.5)	1 (0.8)

[a]Including 2 pts with secondary AML; [b]Thrombocytopenia includes the preferred terms thrombocytopenia and platelet count decreased; [c]Anemia includes the preferred terms anemia, hemoglobin decreased, and red blood cell count decreased; [d]Neutropenia includes the preferred terms neutropenia and neutrophil count decreased.

AML, acute myeloid leukemia; AST, aspartate aminotransferase; COVID-19, corona virus disease 2019; pt(s), patient(s); PTCL, peripheral T-cell lymphoma; R/R, relapsed/refractory; TEAE, treatment-emergent adverse event.

Figure 1

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