# Valemetostat for Patients With Relapsed/Refractory Peripheral T-Cell Lymphomas: The Phase 2 VALENTINE-PTCL01 Trial

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## **PURPOSE**

 To describe the safety, tolerability, and efficacy of valemetostat in patients with relapsed/refractory (R/R) peripheral T-cell lymphoma (PTCL) enrolled in the open-label, single-arm, global, phase 2 VALENTINE-PTCL01 study (DS3201-A-U202; NCT04703192)

## CONCLUSIONS

- Valemetostat demonstrated a high response rate and durable responses in patients with R/R PTCL, who have limited treatment options
- Responses were observed across all PTCL subtypes
- Clinical responses were observed in patients who relapsed or were refractory to their last line of therapy (LOT), and regardless of the number of prior treatments, including those heavily pretreated
- Ten (8.4%) patients treated with valemetostat proceeded to allogeneic hematopoietic cell transplantation (allo-HCT)
- Valemetostat demonstrated an acceptable safety profile
- The most frequently observed treatment-emergent adverse events (TEAEs) were cytopenias
- TEAEs were generally manageable and rarely led to treatment discontinuation



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## INTRODUCTION

- PTCLs account for 10% of non-Hodgkin lymphomas in Western countries and 20% of all lymphomas
- Patients with PTCL typically have poor prognosis, as evidenced by low overall survival (OS) and progression-free survival (PFS) rates<sup>3</sup>
- Over expression of enhancer of zeste homolog (EZH)2, the catalytic subunit of polycomb repressive complex 2, drives the development and progression of many types of cancers, including PTCL<sup>4–7</sup>
- Valemetostat tosylate (valemetostat) is a novel, potent, and selective dual inhibitor of EZH2 and EZH1 approved in Japan at a dose of 200 mg/day for the treatment of R/R PTCL and adult T-cell leukemia/lymphoma<sup>8</sup>

## METHODS

## Study design

- Eligible patients were ≥ 18 years of age, had confirmed PTCL as defined by World Health Organization (WHO) 2016 classification criteria,<sup>9</sup> and had R/R disease after ≥ 1 prior line of systemic therapy
- Patients received valemetostat 200 mg/day in continuous 28-day cycles until disease progression or unacceptable toxicity (Figure 1)

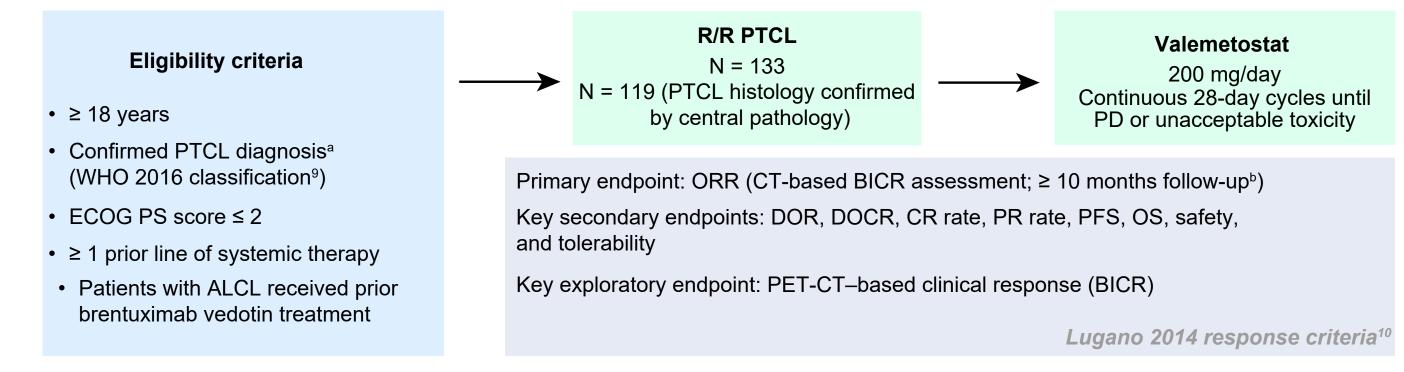
## Efficacy analysis

- The primary endpoint was objective response rate (ORR) by computed tomography (CT)-based blinded independent central review (BICR) assessment according to Lugano 2014 criteria<sup>10</sup>
- Positron emission tomography (PET)-CT-based clinical response assessment (BICR) was an exploratory endpoint

### Safety analysis

The safety and tolerability of valemetostat was a secondary endpoint

## Figure 1. Study design, key inclusion criteria, and endpoints

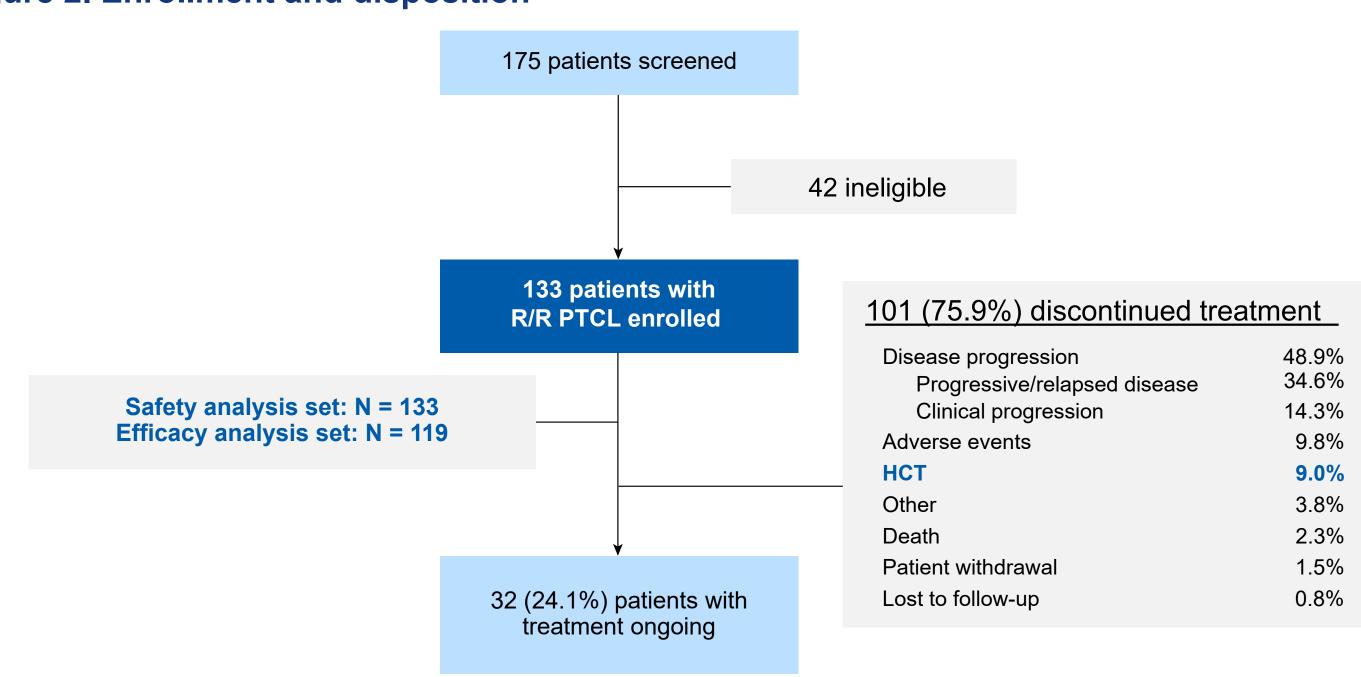


## RESULTS

#### **Patient characteristics**

- Overall, 133 patients with R/R PTCL were included in the study and received ≥ 1 valemetostat dose (Figure 2)
- Median age was 69 (range 22–85) years; most patients (68.4%) were male; the median number of the prior LOTs was 2 (range 1–2); and 26.3% of patients had previously undergone hematopoietic cell transplantation (HCT) (Table 1)
- In total, 119 patients had a confirmed PTCL subtype and were eligible for efficacy analysis The most common PTCL subtypes were AITL (31.6%) and PTCL, NOS (30.8%)

#### Figure 2. Enrollment and disposition



Characteristic	PTCL (N = 133)	
Median age, years (range)	69.0 (22–85)	
Sex, n (%)		
Male	91 (68.4)	
Female	42 (31.6)	
ECOG PS score, n (%)		
0	58 (43.6)	
1	65 (48.9)	
≥ 2	10 (7.6)	
Median prior LOT (range)	2.0 (1–12)	
1	36 (27.1)	
2	36 (27.1)	
≥ 3	61 (45.9)	
Prior HCT, n (%)	35 (26.3)	
Autologous	32 (24.1)	
Allogeneic	5 (3.8)	
PTCL subtypes, n (%)		
TFH phenotype		
AITL	42 (31.6)	
Nodal PTCL with TFH phenotype	8 (6.0)	
FTL	3 (2.3)	
PTCL-NOS	41 (30.8)	
ALCL	7 (5 0)	
ALK <sup>+</sup>	7 (5.3)	
ALK-	2 (1.5)	
MEITL	1 (0.8)	
CD8+ PCAECTCL	1 (0.8)	
PCGTL	1 (0.8)	
Other TCL <sup>a</sup>	13 (9.8)	
Non-TCL or undetermined <sup>b</sup>	6 (4.5)	
Missing <sup>c</sup>	8 (6.0)	

alncludes patients with eligible but undetermined subtypes. Includes patients with undetermined eligibility due to the limited sample tumor tissue. Includes patients with either no

- At the data cut-off date of May 5, 2023, 24.1% (32/133) of patients were still receiving treatment
- Median treatment duration was 18.0 (range 0.3–93.4) weeks

#### **Efficacy**

- In the R/R PTCL efficacy analysis set (N = 119), CT-based ORR was 43.7% (52/119; 95% confidence interval [CI], 34.6–53.1; **Figure 3**)
- Median time to response was 8.1 (range, 5–37) weeks, and median DOR was 11.9 months (95% CI 7.8-not evaluable [NE]; Figure 4)
- ORR per PTCL subtype ranged from 31.7% (PTCL-NOS) to 54.8% (AITL; Figure 5)

#### Figure 3. Clinical response (BICR assessment)

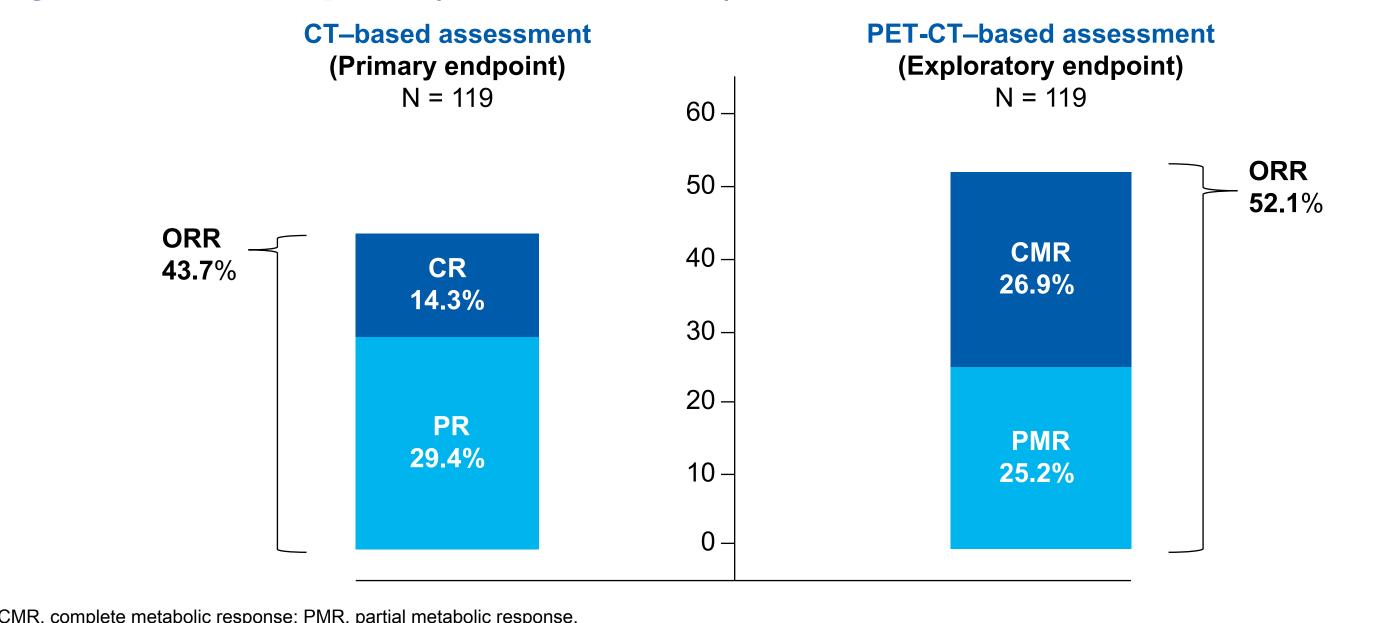
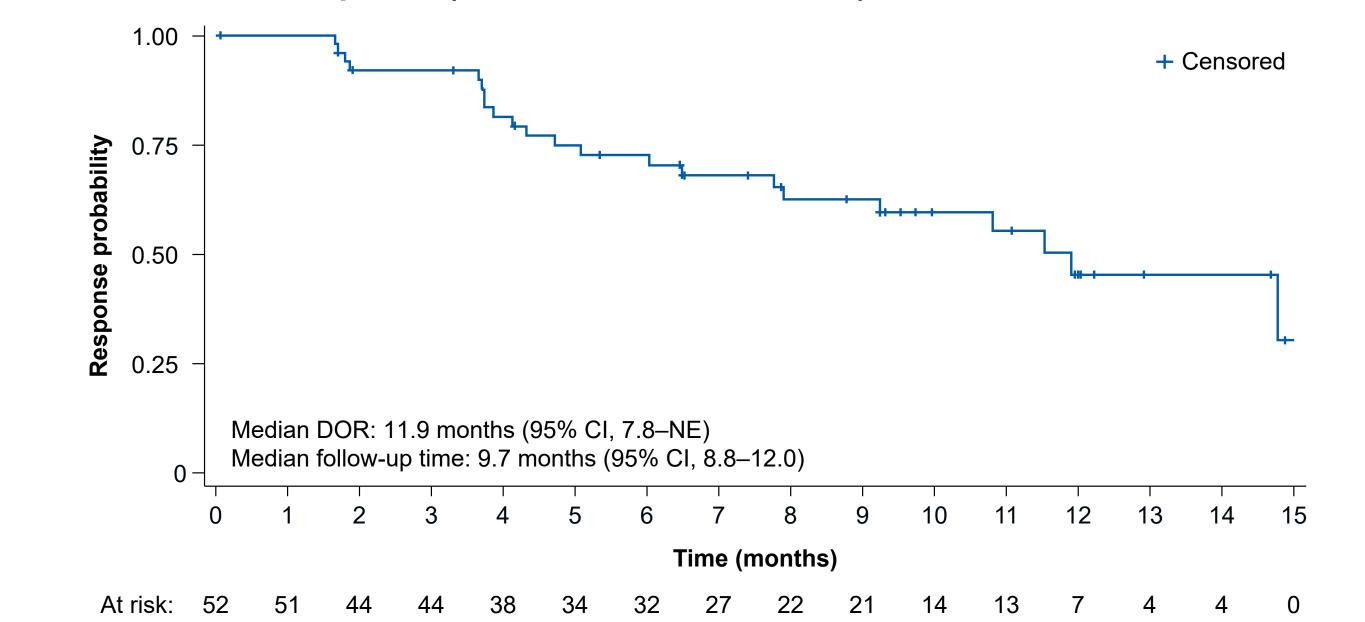


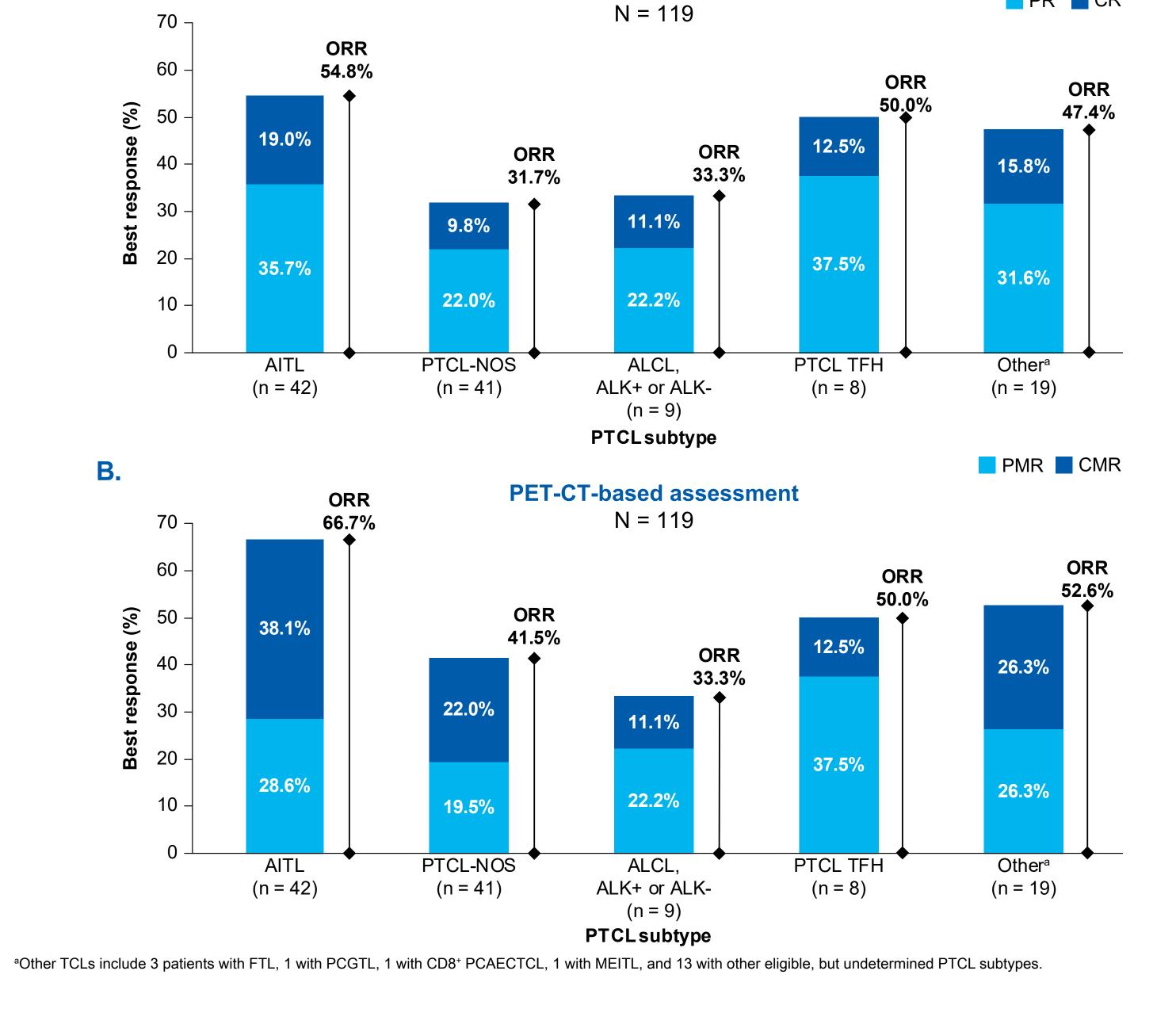
Figure 4. Duration of response (CT-based BICR assessed)



**CT-based assessment** 

PR CR

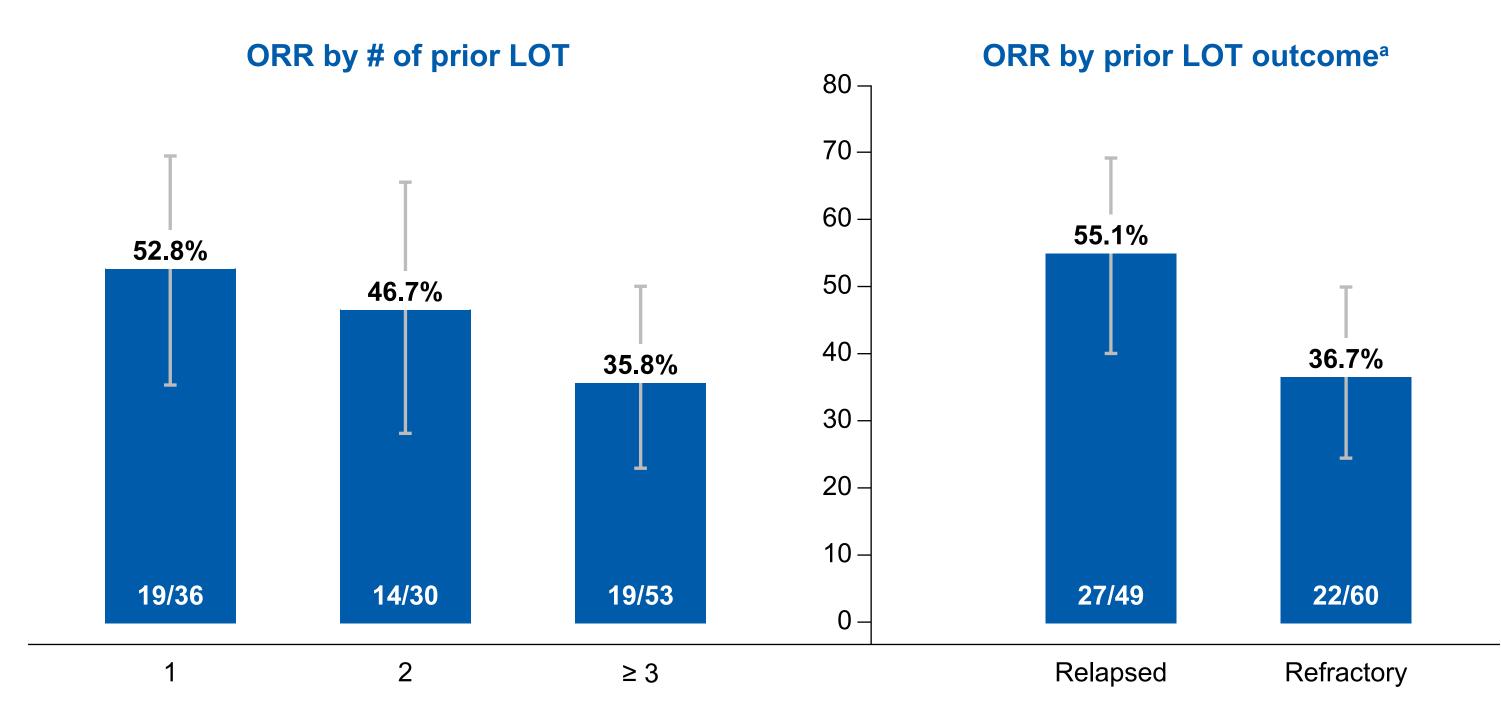
Figure 5. CT-based (A) and PET-CT-based (B) responses by PTCL subtype (BICR assessment)



#### PET-CT-based ORR was 52.1% (62/119; 95% CI, 42.8–61.3; Figure 3)

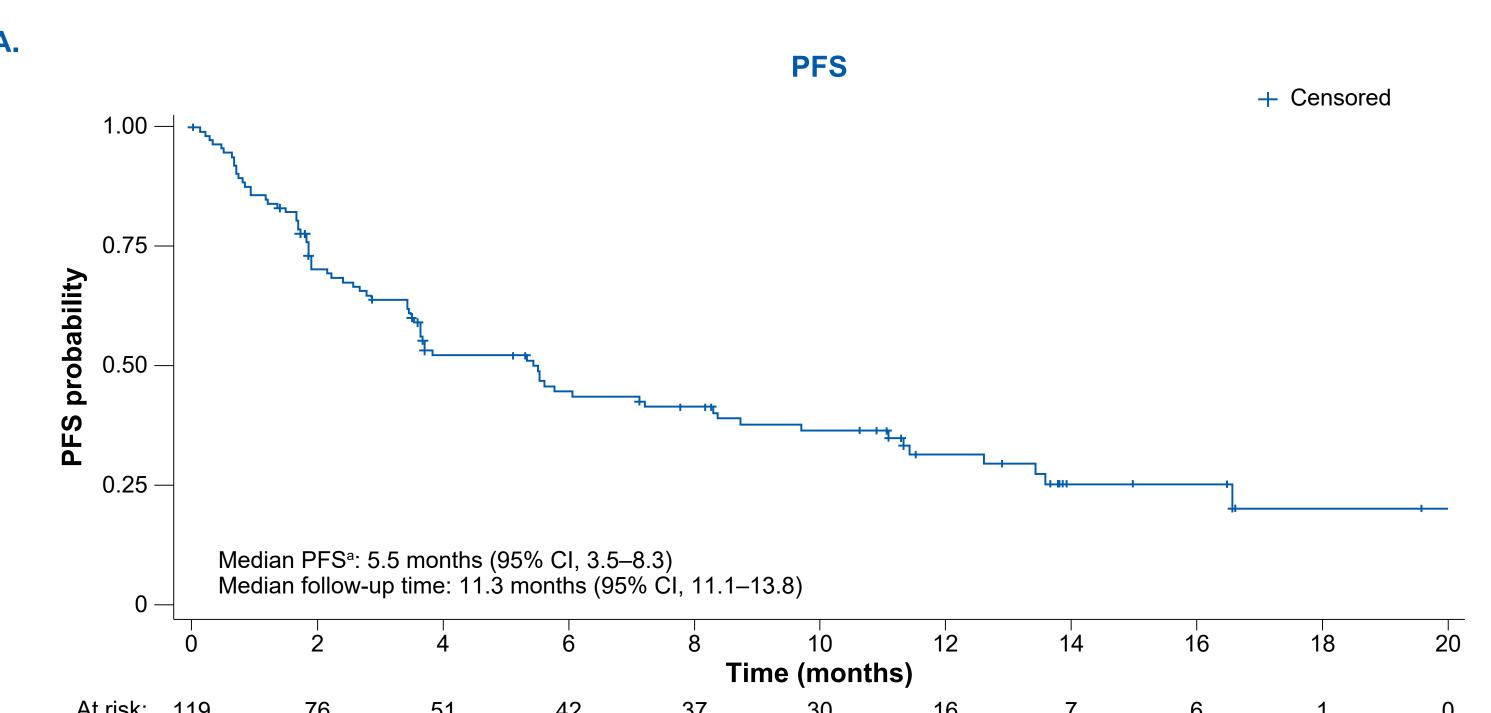
- In total, 26.9% (32/119) achieved CMR
- In total, 25.2% (30/119) achieved PMR
- ORR was nominally better for patients with fewer prior treatment lines (1 vs 2 vs ≥ 3) and for those with relapsed disease (vs refractory) (Figure 6)
- Median CT-based PFS was 5.5 months (95% CI, 3.5–8.3) and median OS was 17.0 months (95% CI, 13.5–NE; **Figure 7**)
- Ten (8.4%) patients treated with valemetostat proceeded to allo-HCT, including 6 patients (5.0%) with CR; median time from first valemetostat dose to subsequent allo-HCT was 6.7 months

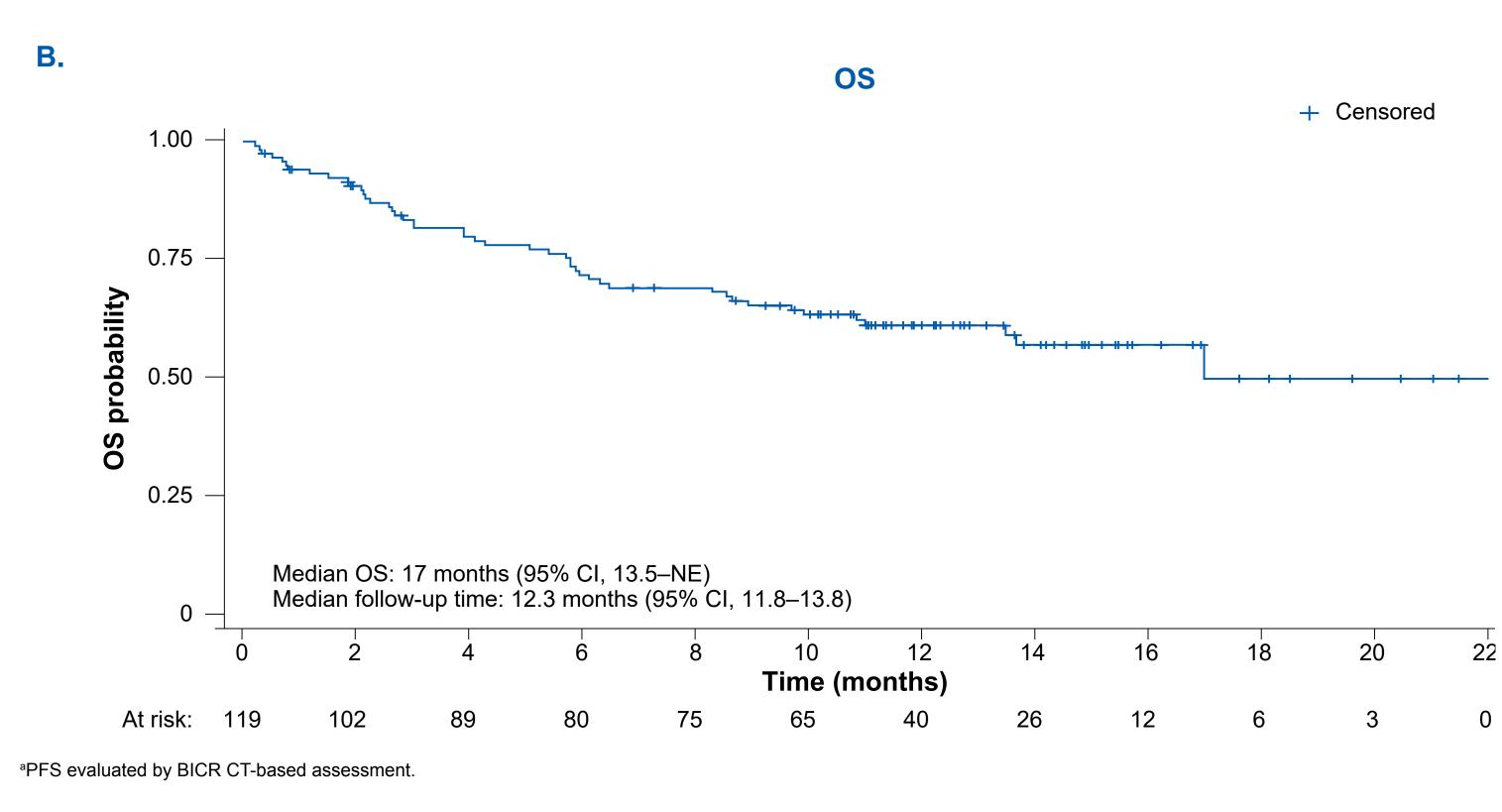
Figure 6. CT-based ORR by number of prior LOTs and last treatment outcome



CR, and patients who had ≥ one prior LOT and did not achieve CR or PR in their latest LOT. Relapsed (including progressed) includes patients that had CR as best response in their latest LOT and relapsed, and patients who had ≥ one prior LOT and had PR as best response in their latest LOT and subsequently progressed.

Figure 7. Kaplan-Meier estimated PFS (A) and OS (B)





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#### Safety and tolerability

- Almost all patients (128/133; 96.2%) experienced ≥ 1 any grade TEAE (Table 2)
- Grade ≥ 3 TEAEs occurred in 57.9% (77/133) of patients
- TEAEs led to treatment discontinuation, dose reduction, or dose interruption in 9.8% (13/133), 15.8% (21/133), and 49.6% (66/133) of patients, respectively (**Table 3**)
- Cytopenias were common (Figure 8), and were manageable with dose modifications and/or supportive
- therapies such as transfusions and granulocyte colony-stimulating factor Thrombocytopenia was the most frequent any grade (49.6%; 66/133) and Grade ≥ 3 (23.3%; 31/133)
- Median time to first onset of Grade ≥ 3 thrombocytopenia (platelet count < 50×10<sup>9</sup>/L) was 18 days
- from first dose Median time to platelet count recovery was 12 days
- Two patients developed secondary acute myeloid leukemia and discontinued treatment

#### **Table 2. TEAE and TRAE summary**

Event, %	PTCL (N = 133)
Any TEAE	96.2
Any TRAE	79.7
Grade ≥ 3 TEAEs	57.9
Grade ≥ 3 TRAEs	36.8
Serious TEAEs	39.8
Serious TRAEs	6.8
EAEs leading to death	11.3
TRAEs leading to death	0
EAEs leading to treatment discontinuation	9.8
TRAEs leading to treatment discontinuation	6.8
EAEs leading to dose reduction	15.8
TRAEs leading to dose reduction	12.0
EAEs leading to dose interruption	49.6
TRAEs leading to dose interruption	31.6
RAF_treatment-related adverse event	

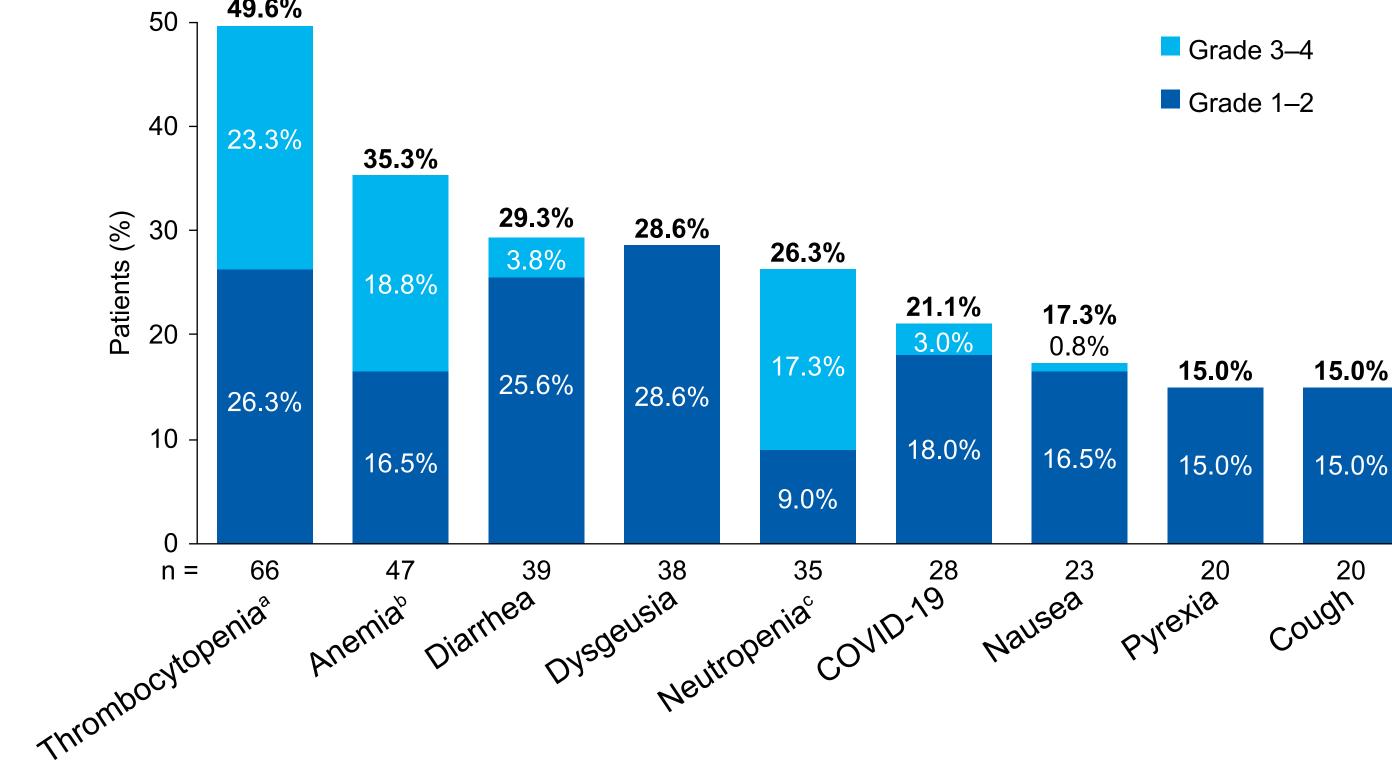
## Table 3. TEAEs that led to dose modifications

**TEAEs** that led to dose modifications<sup>a</sup> (N = 133)

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Treatment discontinuation %	Dose reduction %	Dose interruption %		
9.8	15.8	49.6		
2.3	5.3	16.5		
0	3.8	9.8		
0	1.5	8.3		
0	2.3	5.3		
	Treatment discontinuation %  9.8  2.3  0 0	Treatment discontinuation %         Dose reduction %           9.8         15.8           2.3         5.3           0         3.8           0         1.5		

blood cell count decrease. dNeutropenia includes neutrophil count decrease

#### Figure 8. TEAEs that occurred in ≥ 15% of patients



<sup>a</sup>Thrombocytopenia includes platelet count decrease. <sup>b</sup>Anemia includes hemoglobin decrease, and red blood cell count decrease. <sup>c</sup>Neutropenia includes neutrophil count decrease.

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