Evaluation of PET-CT Metrics and Pharmacokinetics in Adults Receiving Tislelizumab for Relapsed/Refractory Classical Hodgkin Lymphoma: Ancillary Analyses of LYSA Phase 2 TIRHOL Study BGB-A317-210

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CONCLUSIONS

- Tislelizumab is an effective therapeutic option for patients with R/R cHL
- Analyses of centrally reviewed PET-CT imaging demonstrated a trend for underestimation of local response assessments, and therefore in ORR, likely due to the presence of non-lymphomatous inflammatory lesions
- Tislelizumab PK and efficacy outcomes did not differ based on baseline PET-CT metrics
- OS was lower in patients without metabolic response at week 12 compared with patients who had CMR or PMR
- Variations in PET-CT parameters during anti–PD-1 therapy should be interpreted with caution to avoid premature treatment discontinuation

INTRODUCTION

- The phase 2 TIRHOL study (NCT04318080) was designed to evaluate the efficacy of the PD-1 inhibitor tislelizumab in patients with relapsed/refractory (R/R) classical Hodgkin lymphoma (cHL) in Western countries[1]
  - Overall, 45 patients with R/R cHL were treated with tislelizumab every 3 weeks until progressive disease, unacceptable toxicity, or study withdrawal; disease response was assessed by the investigator every 12 weeks per Lugano 2014 positron emission tomography–computed tomography (PET-CT) classification
  - The study met its primary endpoint, with an overall response rate (ORR) of 66.7% (95% CI, 51%-80%) and a complete response rate of 31%
  - Pharmacokinetics (PK) profiles were comparable between BGB-A317-210 and the prior Chinese study BGB-A317-203[2,3]
- Conventional methods using PET-CT to assess lymphoma response are suboptimal in patients treated with PD-1 inhibitors, and specialized criteria are required to prevent premature treatment discontinuation due to inflammation unrelated to disease progression

METHODS

- In this correlative analysis of the TIRHOL study, PET-CT imaging was evaluated post hoc by a central, independent reviewer
- The prognostic role of baseline PET-CT metrics was evaluated with correlation of TMTV4, TLG4, Dmax4, SUVmean, SUVmax, and:
  - First and best response assessments (complete metabolic response [CMR], partial metabolic response [PMR], stable disease [SD], and progressive disease [PD])
  - Outcome: progression-free survival (PFS) and overall survival (OS)
- The longitudinal evolution of TMTV4 during tislelizumab treatment was evaluated
- Tislelizumab PK profiles (cycle 1 postdose and cycle 2 predose concentrations) were evaluated against baseline clinical and PET-CT characteristics

RESULTS

Clinical Characteristics

- PET-CT imaging at baseline and during follow-up was available for central review for 37 of 45 patients included in TIRHOL
- Patient clinical characteristics are shown in **Table 1**

Table 1. Patient Clinical Characteristics

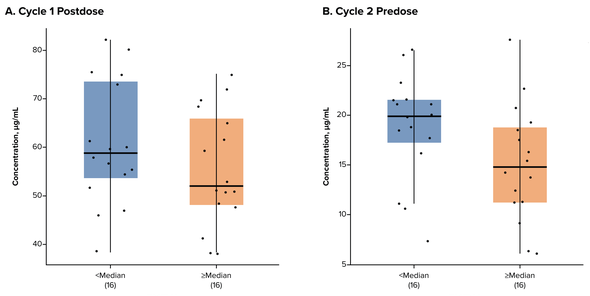
Parameters	Central PET-CT cohort n=37	TIRHOL study cohort n=45
Age, median (range), years	53 (18-87)	64 (18-87)
≥45 years, n (%)	25 (67.6)	31 (68.9)
Male, n (%)	26 (70.3)	30 (66.7)
Time since initial diagnosis, median (range), months	23.5 (6-326)	24.7 (6-326)
ECOG PS 1, n (%)	13 (35.1)	17 (37.8)
IPS ≥3, n (%)	17 (47.2)	22 (50.0)
Refractory status at enrollment, n (%)	12 (32.4)	13 (28.9)
No. of prior lines, median (range)	2 (1-4)	2 (1-4)
Prior therapy, n (%)		
Monoclonal antibody	29 (78.4)	34 (75.6)
Chemotherapy	37 (100)	45 (100)
Radiotherapy	7 (18.9)	10 (22.2)
ASCT	12 (32.4)	14 (31.1)
Other anticancer therapy	0	2 (4.4)
Cohort 1 (prior ASCT and BV)	12 (32.4)	14 (31.1)
Cohort 2 (not candidate for ASCT)	25 (67.6)	31 (68.9)

Abbreviations: ASCT, autologous stem cell transplant ; BV, brentuximab vedotin; ECOG PS, Eastern Cooperative Oncology Group performance status; IPS, International Prognostic Score; PET-CT, positron emission tomography–computed tomography.

Tislelizumab PK Profiles

- No differences in PK results were observed based on key baseline categorical variables (sex, age, B-symptoms, inclusion in cohort 1 or 2, Ann Arbor stage, bulk, refractory vs relapsed disease, International Prognostic Score, TMTV4, albumin level) (**Figure 1**)

Figure 1. Tislelizumab Concentration and TMTV4 at Cycle 1 Postdose and Cycle 2 Predose



Abbreviation: TMTV4, total metabolic tumor volume with standardized uptake value ≥4.

Response Assessments: Local Investigators vs Central Review

- Analyses of PET-CT imaging demonstrated a trend for underestimation of responses assessed by local investigator vs responses by central review in the ORR (66.7% vs 70%) and CMR rate (31% vs 41%), likely due to the presence of non-lymphomatous inflammatory lesions (**Table 2**)
- CMR was achieved in 10 of 45 (22%) included patients at first evaluation at week 12 per local investigator; on central review, the CMR rate was 27% (**Table 3**)

Table 2. Best Response (Primary Endpoint)

n (%)	Best response, local investigators					
Best response, central review	CMR n=11	PMR n=13	SD n=1	PD n=11	NE n=1	All n=37
CMR	10 (90.9)	5 (38.5)	0	0	0	**15 (40.5)**
PMR	1 (9.1)	7 (53.8)	1 (100)	2 (18.2)	0	**11 (29.7)**
SD	0	0	0	1 (9.1)	0	1 (2.7)
PD	0	1 (7.7)	0	8 (72.7)	0	9 (24.3)
NE	0	0	0	0	1 (100)	1 (2.7)

Abbreviations: CMR, complete metabolic response; NE, not evaluated; PD, progressive disease; PMR, partial metabolic response; SD, stable disease.

Table 3. First Response at 12 Weeks

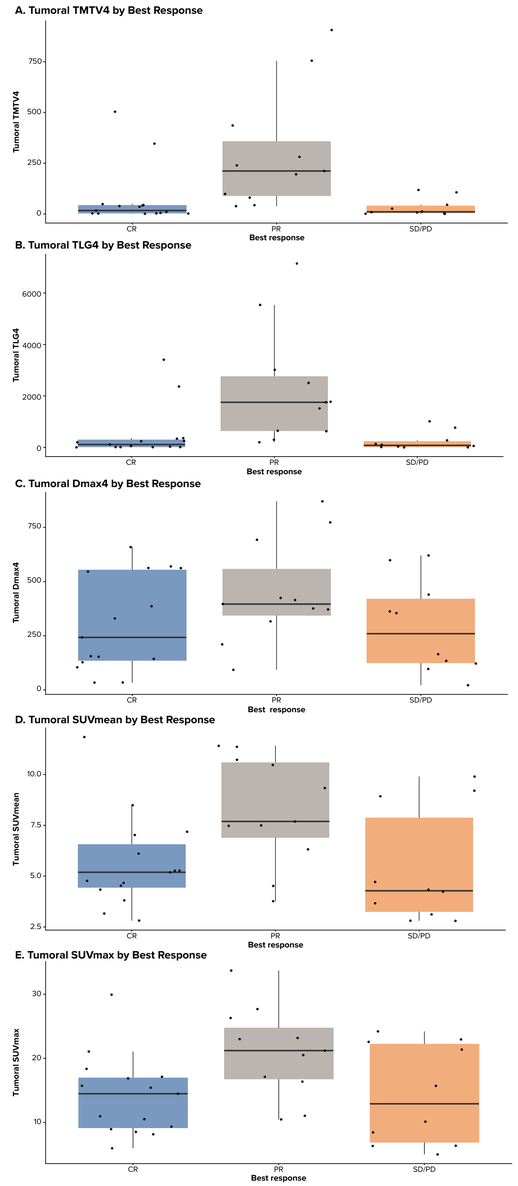
n (%)	First response, local investigators					
First response, central review	CMR n=9	PMR n=11	SD n=1	PD n=14	NE n=1	All n=37
CMR	7 (77.8)	2 (18.2)	1 (50.0)	0	0	**10 (27)**
PMR	2 (22.2)	7 (63.6)	1 (50.0)	3 (21.4)	0	**13 (35)**
SD	0	0	0	1 (7.1)	0	1 (2.7)
PD	0	2 (18.2)	0	10 (71.4)	0	12 (32.4)
NE	0	0	0	0	1 (100)	1 (2.7)

Abbreviations: CMR, complete metabolic response; NE, not evaluated; PD, progressive disease; PMR, partial metabolic response; SD, stable disease.

Baseline PET-CT Metrics and Response

- Median baseline PET-CT metrics were comparable across best metabolic response categories (**Figure 2A-E**)
- Similar results were observed with week 12 metabolic response

Figure 2. Baseline PET-CT Metrics and Best Metabolic Response

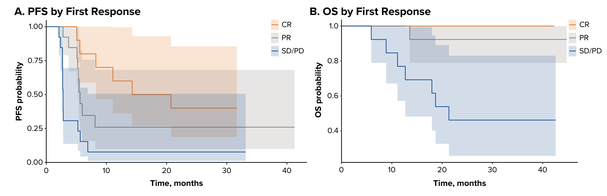


Abbreviations: CR, complete response; Dmax4, maximum distance between lesions with SUV ≥4; PD, progressive disease; PET-CT, positron emission tomography–computed tomography; PR, partial response; SD, stable disease; SUV, standardized uptake value; TLG4, total lesion glycolysis with SUV ≥4; TMTV4; total metabolic tumor volume with SUV ≥4.

PET-CT Metrics and Outcome

- The depth of metabolic response at first evaluation (week 12) influenced PFS and OS and was associated with 1-year PFS rates of 60%, 26%, and 8% (**Figure 3A**) and 1-year OS rates of 100%, 100%, and 77% (**Figure 3B**) in patients with best response of CMR (n=10), PMR (n=13), and NMR (n=13), respectively

Figure 3. PFS and OS by First Metabolic Response

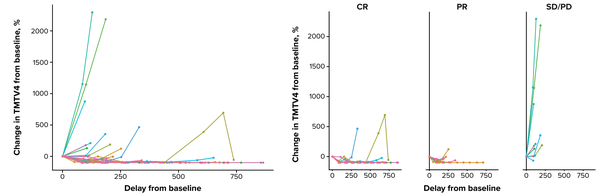


Abbreviations: CR, complete response; OS, overall survival; PD, progressive disease; PET-CT, positron emission tomography–computed tomography; PFS, progression-free survival; PR, partial response; SD, stable disease.

Longitudinal Evaluations of PET-CT Metrics

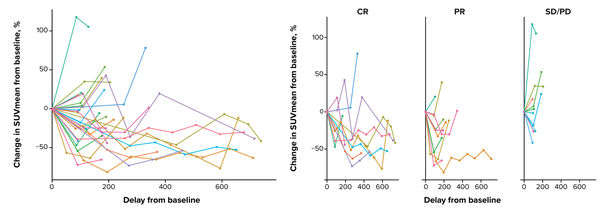
- Longitudinal evaluations of TMTV4 (**Figure 4**) and SUVmean (**Figure 5**) showed a rapid decrease in values at first evaluation in patients with CMR and PMR at week 12
- Patterns of TMTV4 and SUV variations during tislelizumab treatment differed between patients with best metabolic response of CMR, PMR, SD, and PD

Figure 4. TMTV4 (Change From Baseline)



Abbreviations: CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; TMTV4; total metabolic tumor volume with standardized uptake value ≥4.

Figure 5. SUVmean (Change From Baseline)



Abbreviations: CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; SUVmean, mean standardized uptake value.

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DISCLOSURES

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