TISLELIZUMAB (BGB-A317) FOR RELAPSED/REFRACTORY PERIPHERAL T-CELL LYMPHOMAS: SAFETY AND EFFICACY RESULTS FROM A PHASE 2 STUDY

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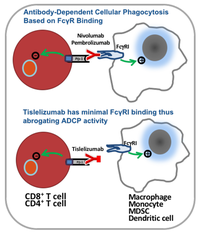
INTRODUCTION

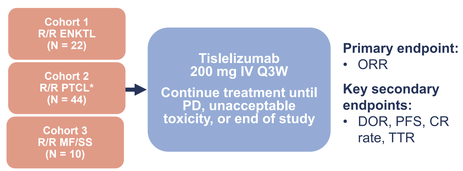
- Peripheral T-cell lymphomas (PTCL) are rare and generally aggressive, and outcomes for patients with relapsed/refractory (R/R) disease are poor.
- The T-cell lymphoma tumor microenvironment has increased programmed death ligand 1 (PD-L1) expression, suggesting PD-1/PD-L1 pathway inhibition may be an effective T-cell lymphoma treatment.
- Binding to FcγR on macrophages compromises antitumor activity of PD-1 antibodies through activation of antibody-dependent macrophage-mediated killing of T effector cells.[1,2]
- Tislelizumab is a humanized IgG4 investigational anti–PD-1 mAb specifically designed to minimize binding to FcγR on macrophages.
- Presented here are the results of a study cohort that evaluated tislelizumab safety and antitumor activity in patients with R/R PTCL (Cohort 2)



mAb, monoclonal antibody; FcγR, Fc region of IgG receptors; IgG, immunoglobulin; PD-1, programmed cell death-1

METHODS

Figure 1. Phase 2, Multicenter, Open-Label Trial



Patients with R/R PTCL (AITL, ALCL, PTCL–NOS):
- Performance status (PS) ≤2
- Measurable disease by CT
- ≥1 previous appropriate combination therapy (eg, CHOP, EPOCH, or similar)
- PD during or after completing the most recent therapy.

Response assessments:
- Responses were assessed by investigator using CT- or PET-based imaging according to the Lugano classification with LYRIC modification.[3]

AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large-cell lymphoma; CR, complete response; DOR, duration of response; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PTCL-NOS, peripheral T-cell lymphoma-not otherwise specified; R/R, relapsed/refractory; TTR, time to response.

RESULTS

Table 1. Patient Disposition and Reasons for Treatment Discontinuation

	Total (N = 44)
Number of patients enrolled	44
Number of patients treated[a] (%)	44 (100)
Patients discontinued from treatment[b], n (%)	38 (86.4)
Reason for discontinuation[b], n (%)	
Progressive disease	28 (63.6)
Adverse event	9 (20.5)
Withdrawal by subject	1 (2.3)
Patients remaining on treatment[b]	6 (13.6)

[a]Percentages are based on number of patients enrolled.
[b]Percentages are based on number of patients treated.

Table 2. Patient and Disease Characteristics

	Total (N = 44)
Median age, years	58
<60 y, n (%)	24 (54.5)
≥60 y, n(%)	20 (45.5)
Gender, n(%)	
Female	15 (34.1)
Male	29 (65.9)
ECOG performance status at baseline, n (%)	
0	21 (47.7)
1	21 (47.7)
2	2 (4.5)
Median time from initial diagnosis to study entry, months (min, max)	14.8 (3.7, 160.6)
Median number of prior regimens, n (min, max)	2 (1, 8)
Stage at study entry, n (%)	
Stage II	8 (18.2)
Stage III	12 (27.3)
Stage IV	24 (54.5)
Country enrollment, n (%)	
China	22 (50.0)
Italy	18 (40.9)
France	3 (6.8)
Taiwan	1 (2.3)

Table 3. Disease Response[a] by PTCL Subtype

	PTCL-NOS (n = 21)	AITL (n = 11)	ALCL (n = 12)	Total (n = 44)
ORR n (%) (95% CI)	5 (23.8) (8.2, 47.2)	2 (18.2) (2.3, 51.8)	2 (16.7) (2.1, 48.4)	9 (20.5) (9.8, 35.3)
CR rate n (%) (95% CI)	3 (14.3) (3.0, 36.3)	0 (0.0) (0.0, 28.5)	0 (0.0) (0.0, 26.5)	3 (6.8) (1.4, 18.7)
DOR (months)				
Median (95% CI)	NE (2.7, NE)	3.2 (NE, NE)	8.3 (8.2, 8.4)	8.2 (2.7, NE)
TTR (months)				
Median (Range)	4.6 (2.8, 5.8)	2.5 (2.1, 2.9)	2.7 (2.7, 2.7)	2.9 (2.1, 5.8)
PFS (months)				
Median (95% CI)	2.7 (2.2, 5.4)	3.4 (1.6, 5.3)	2.7 (1.0, 10.9)	2.7 (2.6, 4.8)

[a]Response criteria: Cheson 2016[3]
NE, not estimable

Table 4. PD-L1 Status and Response

	ORR (95% CI) (%)			
PD-L1 Category[a]	PTCL-NOS (N=14)	AITL (N=8)	ALCL (N=9)	Total (N=31[b])
<25	12.5 (0.3, 52.7)	50.0 (1.3, 98.7)	25.0 (0.6, 80.6)	21.4 (4.7, 50.8)
≥25	16.7 (0.4, 64.1)	16.7 (0.4, 64.1)	0.0 (0.0, 52.2)	11.8 (1.5, 36.4)
<50	11.1 (0.3, 48.2)	25.0 (0.6, 80.6)	16.7 (0.4, 64.1)	15.8 (3.4, 39.6)
≥50	20.0 (0.5, 71.6)	25.0 (0.6, 80.6)	0.0 (0.0, 70.8)	16.7 (2.1, 48.4)
<65	9.1 (0.2, 41.3)	20.0 (0.5, 71.6)	12.5 (0.3, 52.7)	12.5 (2.7, 32.4)
≥65	33.3 (0.8, 90.6)	33.3 (0.8, 90.6)	0.0 (0.0, 97.5)	28.6 (3.7, 71.0)

[a]PD-L1Category - % cells expressing PD-L1 by IHC
[b]Only 31 of 44 cohort 2 patients had sufficient sample for PD-L1 testing

Figure 2. Duration of Treatment and Time to Response

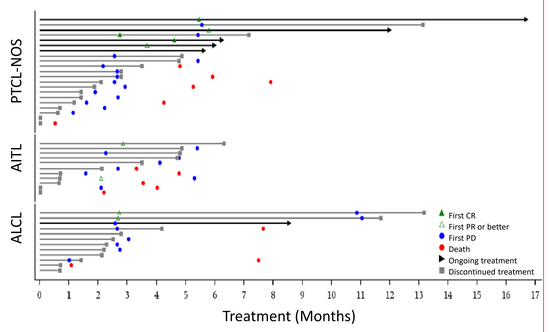


Figure 3. Progression-Free Survival

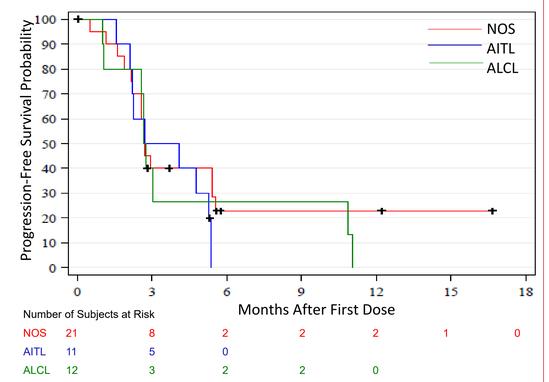


Table 5. Summary of Treatment-Emergent Adverse Events (TEAEs)

Event, n (%)	N = 44
Grade ≥3 TEAEs	23 (52.3)
Serious TEAEs	21 (47.7)
TEAEs leading to treatment discontinuation	8[a] (18.2)
TEAEs leading to death	3[b] (6.8)
Immune-related (ir) TEAEs[c]	18 (40.9)
Pruritis	5 (11.4)
Erythema	2 (4.5)
Hyperthyroidism	2 (4.5)
Hypothyroidism	2 (4.5)
Rash pruritic	2 (4.5)

[a]Cancer pain, death, dyspnea, general physical health deterioration, hemophagocytic lymphohistiocytosis, intussusception, multiple organ dysfunction syndrome, pancytopenia.
[b]General physical health deterioration (n=1), death (n=1), and multiple organ dysfunction syndrome (n=1); all likely related to disease progression.
[c]irAEs were all grade 1 or 2 except one event of grade 3 erythema.

CONCLUSIONS

- Tislelizumab is an investigational anti–PD-1 mAb specifically designed to minimize binding to FcγR on macrophages.
- Tislelizumab was generally well tolerated, and the safety profile was similar to that of other anti–PD-1 antibodies.
- Tislelizumab showed modest activity in patients with R/R PTCL.
- Higher PD-L1 expression may lead to increased response in PTCL-NOS patients, but small numbers limit conclusions.
- Future development in this aggressive disease should consider a mechanism-based combination to drive more rapid, deep, and sustainable responses.

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