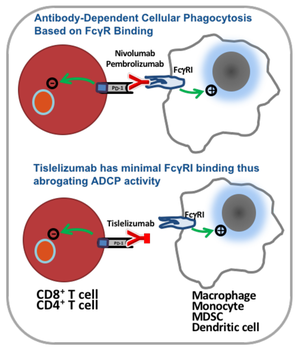
Results of Tislelizumab Monotherapy in Chinese Patients With Relapsed or Refractory Classical Hodgkin Lymphoma: A Single Arm, Multicenter, Pivotal Phase 2 Study

Yuqin Song, MD, PhD,[1] Quanli Gao, MD,[2] Huilai Zhang, MD, PhD,[3] Lei Fan, MD, PhD,[4] Jianfeng Zhou, PhD,[5] Dehui Zou, MD,[6] Wei Li, MD,[7] Haiyan Yang, PhD,[8] Ting Liu, MD, PhD,[9] Quanshun Wang, MD, PhD,[10] Fangfang Lv, MD,[11] Yu Yang, MD,[12] Haiyi Guo, MD,[13] Liudi Yang, MD,[13] Rebecca Elstrom, MD,[13], Jane Huang, MD,[13] William Novotny, MD,[13] Vivian Wei, PhD,[13] and Jun Zhu, MD[1]

[1]Key laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Lymphoma, Peking University Cancer Hospital & Institute; [2]Department of Immunotherapy, Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China; [3]Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, Tianjin's Clinical Research Center for Cancer, Tianjin, China; [4]Department of Hematology, the First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, Collaborative Innovation Center for Cancer Personalized Medicine, Nanjing, China; [5]Department of Hematology, Tongji Hospital, Tongji Medical College, Wuhan, China; [6]State Key Laboratory of Experimental Hematology, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China; [7]Department of Hematology, Cancer Center, The First Hospital of Jilin University, Changchun, China; [8]Department of Oncology, Zhejiang Cancer Hospital, Hangzhou, China; [9]Department of Hematology, West China Hospital of Sichuan University, Chengdu, China; [10]Department of Hematology, Chinese PLA General Hospital, Beijing, China; [11]Department of Medical Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; [12]Department of Lymphoma and HNC, Fujian Cancer Hospital, Fujian, China; [13]BeiGene (Beijing) Co., Ltd., Beijing, China and BeiGene USA, Inc., San Mateo, CA, USA

INTRODUCTION

- Patients with relapsed or refractory classical Hodgkin lymphoma (cHL) who have failed HDT/ASCT, or have chemo-resistant disease and are not candidates for HDT/ASCT, have a very poor prognosis.
- Anti-PD-1 Abs, including nivolumab and pembrolizumab, are active in this setting. However, only a minority of patients achieve durable complete remissions.
- 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 Ab specifically designed to minimize binding to FcγR on macrophages.

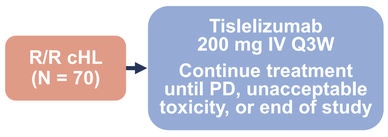


- Presented here are the results of a pivotal Phase 2 trial of tislelizumab in Chinese patients with cHL who have either failed or are not candidates for HDT/ASCT.

Ab, antibody; ASCT, autologous stem cell transplantation; FcγR, Fc region of IgG receptors; HDT, high-dose therapy; IgG, immunoglobulin; PD-1, programmed cell death-1.

METHODS

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



Primary endpoint:
- ORR assessed by IRC

Key Secondary endpoints:
- DOR, PFS, CR rate, TTR

Patients with R/R cHL:

- Failed to achieve a response or progressed after ASCT
  or
- Received ≥2 prior lines of systemic therapy for cHL and was not an ASCT candidate

Response assessments:

- Responses were assessed by IRC using PET-based imaging according to the Lugano Classification.[3]

cHL, classical Hodgkin lymphoma; CR, complete response; DOR, duration of response; IRC, independent review committee; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; R/R, relapsed/refractory; TTR, time to response.

RESULTS

Data cut: Nov 26, 2018

Table 1. Patient and Disease Characteristics

Baseline Characteristics	Total (N = 70)
Age (years), median (range)	32.5 (18, 69)
Age group <65 / 65-74 years, n (%)	66 (94.3) / 4 (5.7)
Sex, male / female, n (%)	40 (57.1) / 30 (42.9)
Time since first diagnosis of cHL (months), median (range)	25.33 (4.6, 262.3)
Stage IV at study entry, n (%)	42 (60.0)
Bulky disease*, n (%)	8 (11.4)
Bone marrow involvement, n (%)	22 (31.4)
B symptom(s), n (%)	26 (37.1)
Ineligible for prior ASCT†, n (%)	
Failure to achieve an objective response to salvage chemotherapy	53 (75.7)
Inadequate stem cell collection or unable to collect stem cells	2 (2.9)
Comorbidities	2 (2.9)
Prior lines of systemic therapy, median (range)	3 (2-11)
Type of prior therapy, n (%)	
Chemotherapy	70 (100.0)
Radiotherapy	21 (30.0)
ASCT	13 (18.6)
Immunotherapy‡	15 (21.4)
Brentuximab vedotin	4 (5.7)

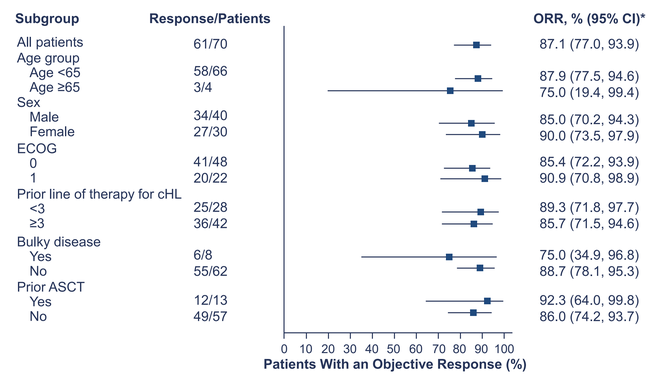
*Mediastinal mass ratio of 0.33 or size of any single node/nodal mass ≥10 cm in diameter.
†All received ≥2 prior regimens.
‡Immunotherapy included brentuximab vedotin, rituximab, cytokine-induced killer cell transfusion, thalidomide, and lenalidomide.

Table 2: Efficacy: Best Overall Response by IRC

Best Response*, n (%)	N = 70
ORR (CR+PR), n (%) [95% CI]†	61 (87.1) [77, 93.9]
Complete response	44 (62.9)
Partial response	17 (24.3)
Stable disease	3 (4.3)
Progressive disease	5 (7.1)
Died before any post-baseline tumor assessment‡	1 (1.4)

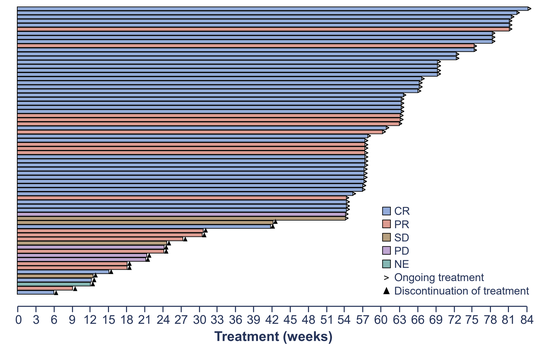
*Response criteria: Lugano 2014.
†1-sided Clopper-Pearson 95% CI.
‡Died due to disease progression, not related to study drug.

Figure 2. Forest Plot of ORR Based on IRC by Subgroup



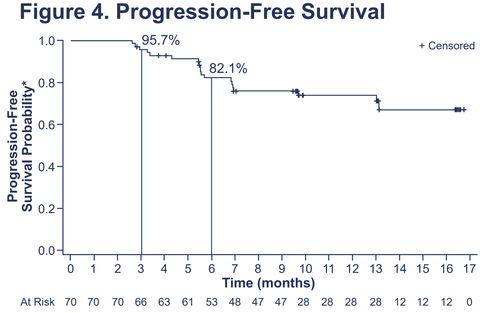
*2-sided Clopper-Pearson 95% CIs.

Figure 3. Duration of Treatment and Time to Response



- The majority of patients achieved a response by the first response assessment.

Figure 4. Progression-Free Survival



- Median PFS has not been reached.
- Median PFS follow-up duration was 13 months.

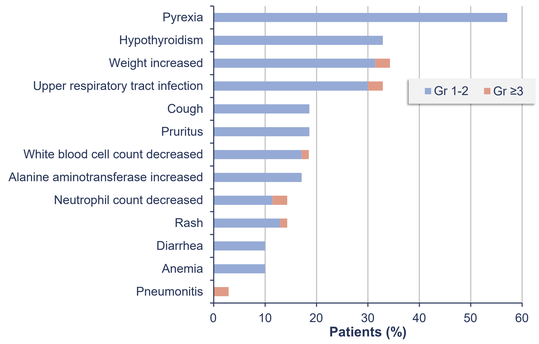
*Kaplan-Meier estimate.

Table 3. Summary of Treatment-Emergent Adverse Events

Event, n (%)	N = 70
Grade ≥3 TEAE	21 (30)
Serious TEAE	12* (17.1)
TEAE leading to treatment discontinuation	4† (5.7)
TEAE leading to death	0 (0.0)
Immune-related (ir) TEAEs (by aggregate category)	
≥1 irTEAE	27 (38.6)
Thyroid disorder	16 (22.9)
Pneumonitis	5 (7.1)
Skin adverse reactions	6 (8.6)
Myositis/rhabdomyolysis/cardiomyopathy‡	1 (1.4)
Nephritis and renal dysfunction	1 (1.4)
Other immune-related reactions (lipase increased)	1 (1.4)

*SAEs in all 11 patients determined to be possibly related to tislelizumab.
†Pneumonitis (n = 2), focal segmental glomerulosclerosis (n = 1), organizing pneumonia (n = 1).
‡Blood creatine phosphokinase increased.

Figure 5. TEAEs in ≥10% of Patients or Grade ≥3 TEAEs in ≥2 Patients Regardless of Causality



TEAE, treatment-emergent adverse events by individual preferred term.

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 for the treatment of cHL.
- Tislelizumab was shown to be highly active in patients with R/R cHL who failed or were ineligible for ASCT, as demonstrated by:
  - High ORR and CR rates (87% and 63%, respectively)
  - Median duration of response has not been reached

REFERENCES

1. Dahan R. et al. *Cancer Cell*. 2015;28:285-295.
2. Arlauckas S. et al. *Sci Transl Med*. 2017; 9(389): eeal3504.
3. Cheson BD et al. *J Clin Oncol*. 2014;32(27):3059-3067

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