Title: Tislelizumab (BGB-A317) for relapsed/refractory (R/R) classical hodgkin lymphoma (cHL): long-term follow-up efficacy and safety results from a phase 2 study

---

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

Author Affiliations:
[1]Department of Lymphoma, Peking University Cancer Hospital & Institute (Beijing Cancer Hospital), Beijing, China; [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 Lymphoma, Cancer Hospital of the University of Chinese Academy of Sciences, 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]BeiGene (Beijing) Co., Ltd., Beijing, China, and BeiGene USA, Inc., San Mateo, CA, USA

Background: Tislelizumab is a humanized IgG4 monoclonal antibody with high affinity/specificity for programmed cell death protein 1 (PD-1). It was engineered to minimize binding to Fc-γ receptors on macrophages, thereby decreasing antibody-dependent phagocytosis, a potential mechanism of T-cell clearance and resistance to anti–PD-1 therapy. Tislelizumab therapy was highly active in autologous stem cell transplant (ASCT)-failed or ineligible patients with R/R cHL (*Leukemia*. 2020;34:533). Here we report results from up to 3 years follow-up.

Methods: This a single-arm, multicenter phase 2 study (NCT03209973) of 200 mg tislelizumab administered intravenously to patients (pts) with R/R cHL every 3 weeks until progressive disease (PD) or unacceptable toxicity. Patients were eligible if they: failed to achieve a response or progressed after ASCT, or: received ≥2 lines of prior systemic chemotherapy for cHL and were ineligible for ASCT. Primary endpoint was overall response rate (ORR) assessed by an

independent review committee (IRC) per Lugano criteria (*J Clin Oncol*. 2014;32:3059). Secondary endpoints were progression-free survival (PFS), duration of response (DOR), complete response (CR) rate, and time to response (TTR) per IRC, safety, and tolerability.

Results: Pts (N=70) from 11 centers in China were enrolled and treated; characteristics have been previously reported. As of the data cutoff date (Nov 2, 2020), median follow-up was 33.8 months (range, 3.4-38.6). Pts still on treatment at the end of study (n=33; 47.1%) entered a long-term extension study. Efficacy data is presented in the Table below. In the 13 pts who received prior ASCT, 11 (86.6%) achieved CR. The most common treatment-emergent adverse events (AEs; ≥30%) were pyrexia (57.1%), upper respiratory tract infection (URTI; 38.6%), hypothyroidism (37.1%), and increased weight (34.3%). Treatment-related grade ≥3 AEs (≥2 pts) were URTI, pneumonitis, hypertension, neutropenia, lipase increased, weight increased, and increased creatine phosphokinase (CPK; 2.9% each). Immune-related AEs were reported in 32 pts (45.7%), with grade ≥3 AEs in 8 pts (11.4%): pneumonitis (4) and skin adverse reactions, nephritis, lipase increased, and blood CPK increased (1 each). AEs led to treatment discontinuation in 6 pts (10%).

Conclusions: Long-term follow-up of R/R cHL pts treated with tislelizumab further demonstrated the substantial therapeutic activity and continued PFS benefit. There were no new safety concerns identified for long-term treatment with tislelizumab.

Table

	N=70	**95% CI**
ORR, n (%)	61 (87.1)	77.0, 93.9*
CR, n (%)	47 (67.1)	54.9, 77.9*
mDOR[†], mo	31.3	20.73, NE
mPFS[†], mo	31.5	16.53, NE
mOS[†], mo	Not reached	NE, NE
24-mo event free rate, %	93.9	84.5, 97.7

m, median; NE, not estimable; OS, overall survival.

*Two-sided Clopper-Pearson 95% CI. [†] Based on Kaplan-Meier estimation.