Connecting Hematology - For Clinical and Research Excellence

Tislelizumab (BGB-A317) for Relapsed/Refractory Classical Hodgkin Lymphoma: Long-term Follow-up Efficacy and Safety Results From a Phase 2 Study

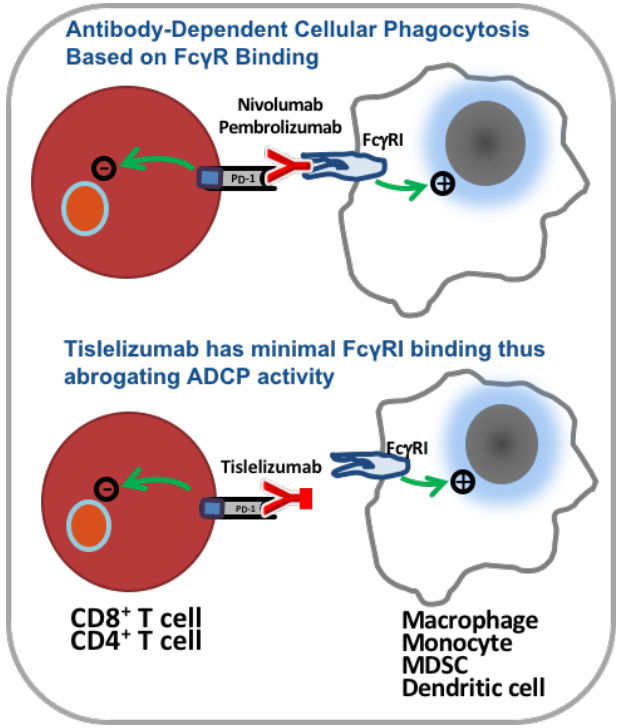
Yuqin Song, MD, PhD[1]; Quanli Gao, MD[2]; Huilai Zhang, MD, PhD[3]; Lei Fan, MD, PhD[4]; Jianfeng Zhou, MD, PhD[5]; Dehui Zou, MD[6]; Wei Li, MD[7]; Haiyan Yang, MD, PhD[8]; Ting Liu, MD, PhD[9]; Quanshun Wang, MD, PhD[10]; Fangfang Lv, MD[11]; Haiyi Guo, MD[12]; Xia Zhao, MD[12]; Jane Huang, MD[12];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

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

June 11, 2021
Hodgkin lymphoma – Clinical (Abstract **S207**)

BACKGROUND

- Patients with R/R cHL who have failed HDT/ASCT or have chemotherapy-resistant disease and are not candidates for HDT/ASCT have a very poor prognosis[1-4]
- Anti-PD-1 Abs, including nivolumab and pembrolizumab, are active in this setting[5,6]; however, only a minority of patients achieve durable complete remissions[7,8]
- Binding to FcγR on macrophages compromises anti-tumor activity of PD-1 antibodies through activation of antibody-dependent macrophage-mediated killing of effector T cells[9,10]
- Tislelizumab is a humanized IgG4 anti-PD-1 Ab, specifically engineered to minimize binding to FcγR on macrophages[11]



- Presented here are the long-term follow-up data of a pivotal phase 2 trial of tislelizumab in Chinese patients with R/R cHL who have either failed or who are not candidates for HDT/ASCT

Ab, antibody; cHL, classical Hodgkin lymphoma; FcγR, Fc region of IgG receptors; HDT/ASCT, high-dose chemotherapy and autologous stem cell transplant; IgG, immunoglobulin G; PD-1, programmed cell death-1; R/R, relapsed or refractory.

1 Josting A, et al. *Blood*. 2000;96:1280-1286. 2. Ansell SM, et al. *Am J Hematol*. 2012;87:1096-1103. 3. Bonfante V, et al. *J Clin Oncol*. 1997;528-534. 4. Longo DL, et al. *J Clin Oncol*. 1992;210-8. 5. Ansell SM, et al. *N Engl J Med*. 2015;372:311-319. 6. Chen R, et al. *J Clin Oncol*. 2017;35:2125-2132. 7. Armand P, et al. *J Clin Oncol*. 2016;34:3733-3739. 8. Younes A, et al. *Lancet Oncol*. 2016;17:1283–1294. 9. Dahan R. et al. *Cancer Cell*. 2015;28:285-295. 10. Arlauckas S, et al. *Sci Transl Med*. 2017;9(389):eeal3504. 11. Liu S-Y, et al. *Expert Opin Investig Drugs*. 2020:29:1355-1364.

STUDY OVERVIEW

BGB-A317-203: A Multicenter, Single-Arm Trial[1]

R/R cHL (N=70)

Tislelizumab
200 mg IV Q3W

Continue treatment until PD, unacceptable toxicity, or end of study

Primary endpoint:
- ORR assessed by IRC based on PET/CT per Lugano criteria[2]

Key secondary endpoints:
- DOR, PFS, CR rate, and TTR by IRC; safety endpoints

Exploratory endpoints:
- OS, biomarkers

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 were not an ASCT candidate

Study follow-up time

- Median 33.8 months (range, 3.4-38.6 months)

ASCT, autologous stem cell transplant; cHL, classical Hodgkin lymphoma; CR, complete response; DOR, duration of response; IRC, independent review committee; IV, intravenous; ORR, overall response rate; OS, overall survival; PD, progressive disease; PET, positron emission tomography; PFS, progression-free survival; Q3W, every 3 weeks; R/R, relapsed or refractory; TTR, time to response.

1. Song YQ, et al. *Leukemia.* 2020;34(2):533-542. 2. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-3067.

PATIENT CHARACTERISTICS

Baseline Characteristics	Total (N=70)
Median age (range), years	32.5 (18–69)
Age group, n (%)	
<65 years	66 (94.3)
≥65 years	4 (5.7)
Sex, n (%)	
Male	40 (57.1)
Female	30 (42.9)
ECOG performance status, n (%)	
0	48 (68.6)
1	22 (31.4)
Stage IV at study entry, n (%)	42 (60.0)
Bulky disease[a], n (%)	8 (11.4)
Bone marrow involvement, n (%)	22 (31.4)
B-symptom(s), n (%)	26 (37.1)
Median time from initial diagnosis (IQR), months	25.33 (12.91–40.54)
Prior lines of systemic therapy, median (range)	3 (2–11)
Type of prior therapy, n (%)	
Chemotherapy	70 (100.0)
ASCT	13 (18.6)
Immunotherapy[b]	15 (21.4)
Brentuximab vedotin	4 (5.7)
Ineligible for prior ASCT[c], n (%)	57 (81.4)
Patients with prior radiation therapy, n (%)	21 (30.0)

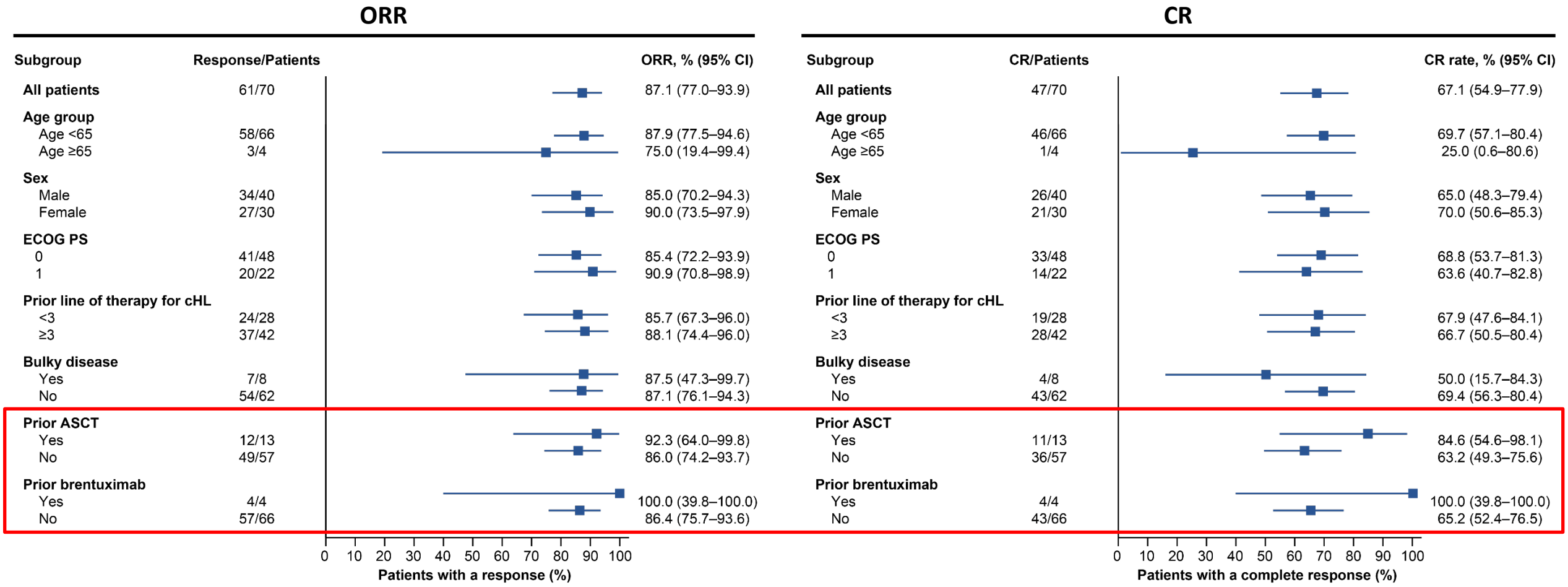
ASCT, autologous hematopoietic stem cell transplant; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range.
[a]Mediastinal mass ratio of 0.33 or size of any single node/nodal mass ≥10 cm in diameter. [b]Included brentuximab vedotin, rituximab, cytokine-induced killer cell transfusion, thalidomide, and lenalidomide. [c]Patients were ineligible for ASCT if they did not achieve at least a partial response to salvage chemotherapy, were ≥65 years of age, had contraindicating comorbidities, or due to the failure or inability to collect hematopoietic stem cells. All received ≥2 prior regimens.

BEST OVERALL RESPONSE BY IRC

Best response[a], n (%)	N=70
ORR	**61 (87.1)**
(95% CI[b])	**(77.0–93.9)**
CR	47 (67.1)
(95% CI[b])	(54.9–77.9)
PR	14 (20.0)
SD	2 (2.9)
PD	6 (8.6)
Died before any postbaseline tumor assessment[c]	1 (1.4)

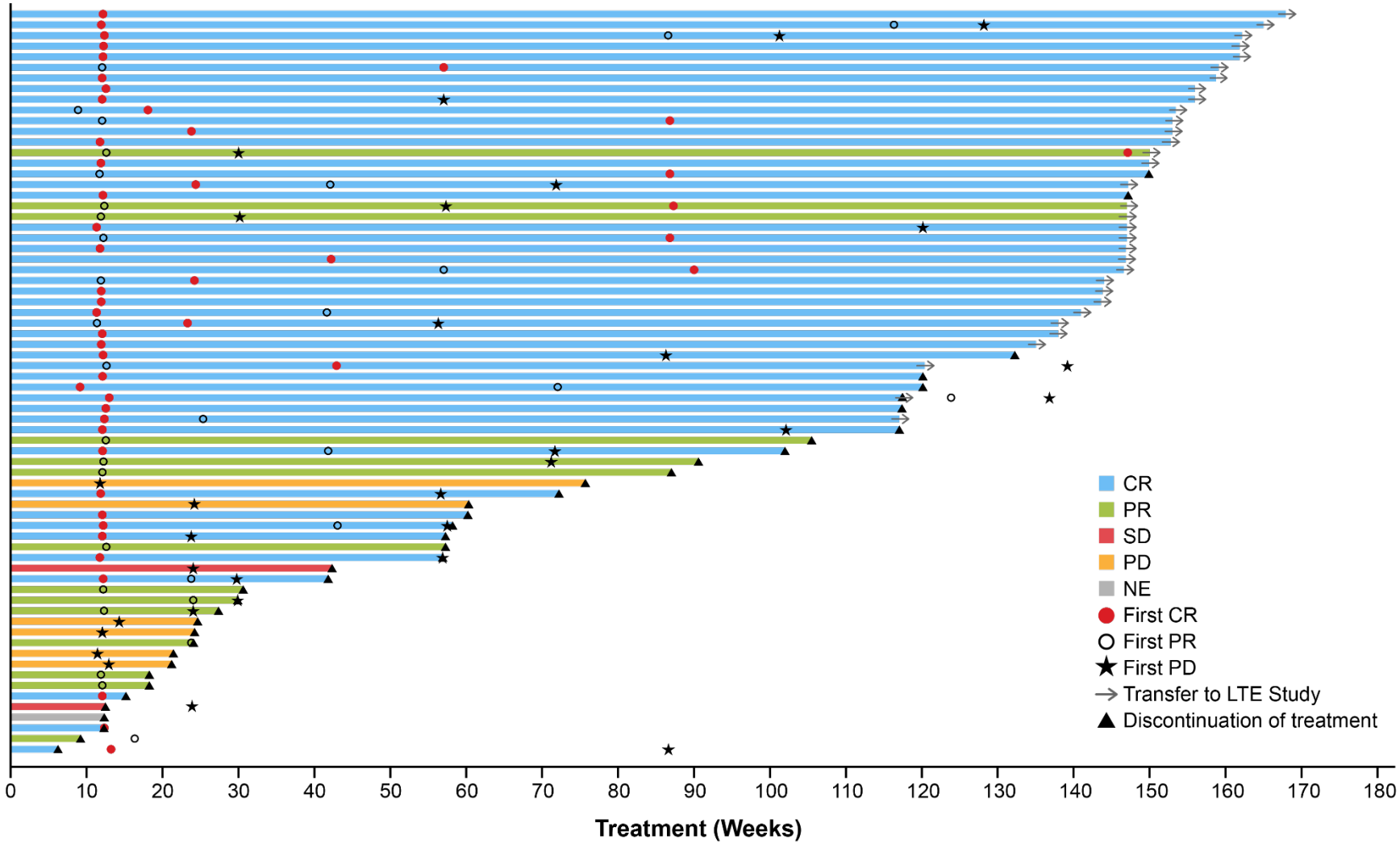
CR, complete response; IRC, independent review committee; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Response assessment according to the Lugano Classification.[1] [b]1-sided Clopper-Pearson 95% CI. [c]Died due to disease progression, not related to study drug.
1. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-3067.

RESPONSES BY SUBGROUP ANALYSIS



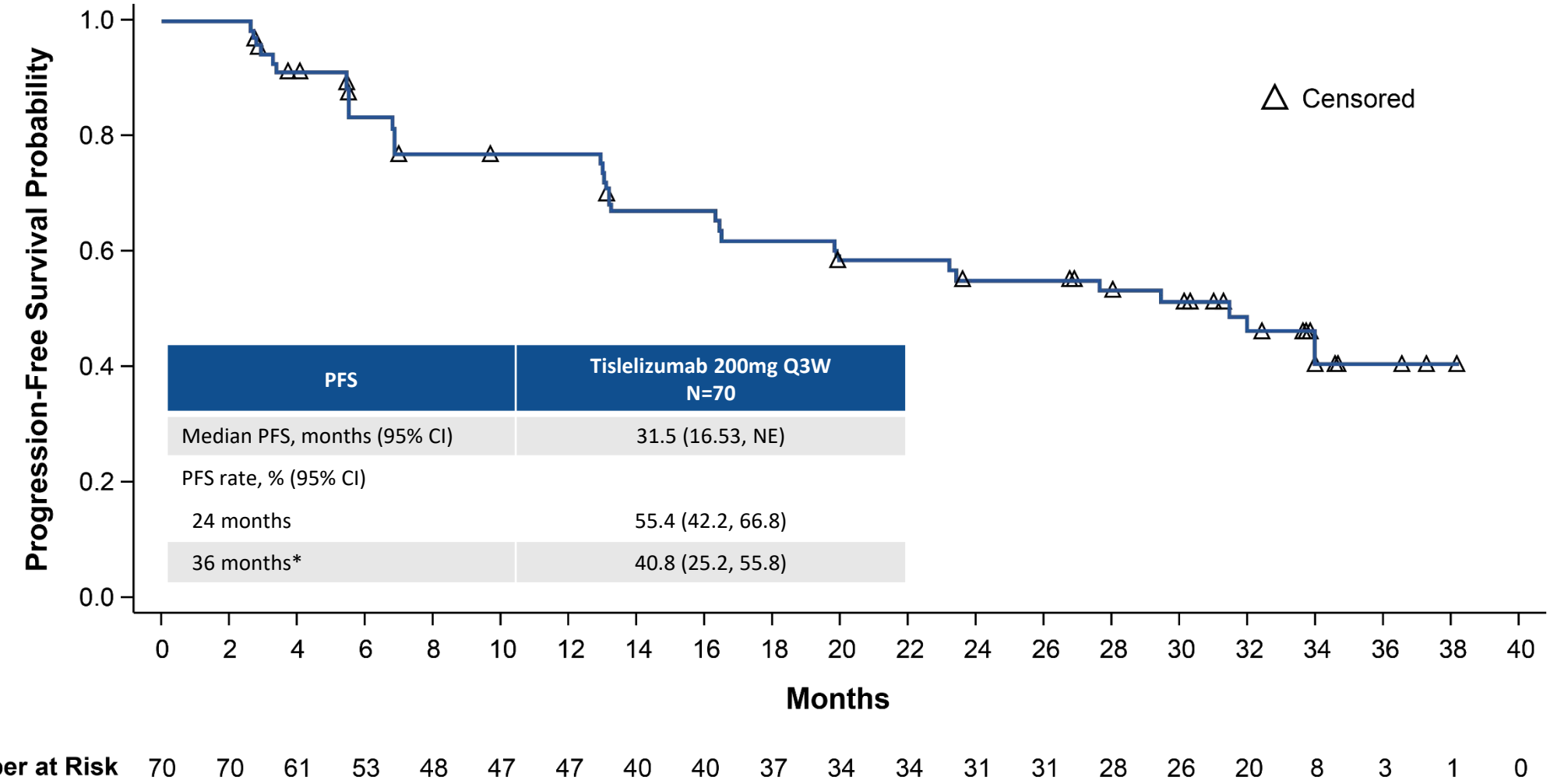
ASCT, autologous stem cell transplant; cHL, classical Hodgkin Lymphoma; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, overall response rate.
Note: 95% CIs were calculated using the 2-side Clopper-Pearson method.

DURATION OF TREATMENT & TIME TO RESPONSE



CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

PFS

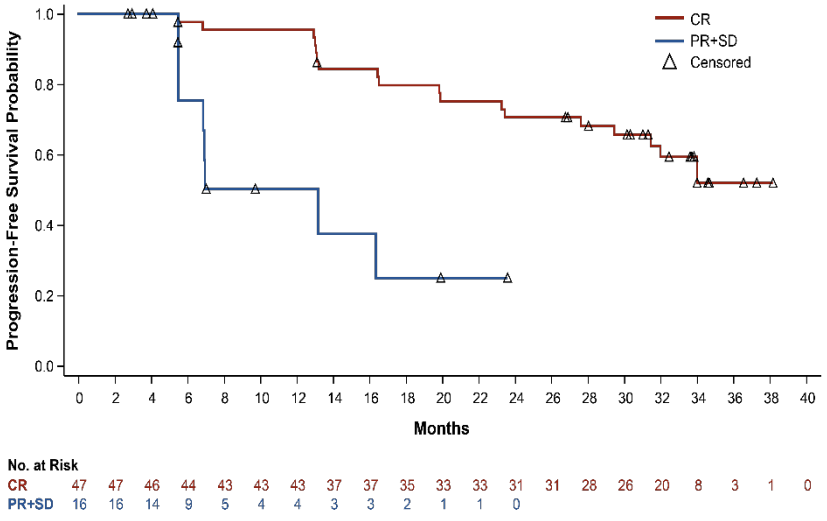


PFS	Tislelizumab 200mg Q3W N=70
Median PFS, months (95% CI)	31.5 (16.53, NE)
PFS rate, % (95% CI)	
24 months	55.4 (42.2, 66.8)
36 months*	40.8 (25.2, 55.8)

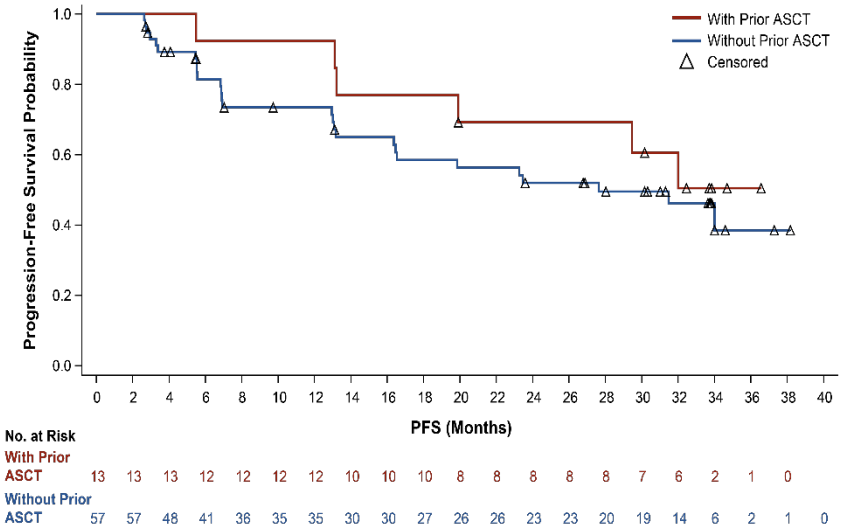
NE, not estimable; PFS, progression-free survival; Q3W, every 3 weeks.
*Note: Data to be interpretated with caution due to smaller subject number at risk.

PFS BY SUBGROUP

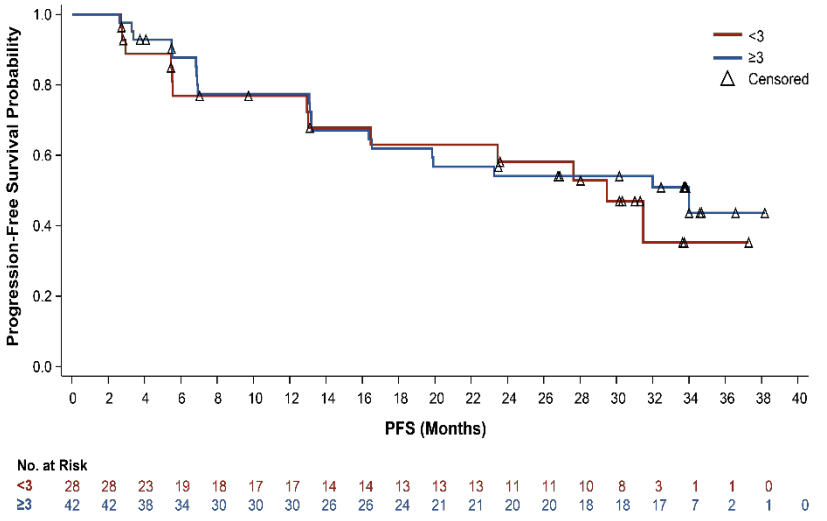
BOR



Prior ASCT



Prior lines of therapy



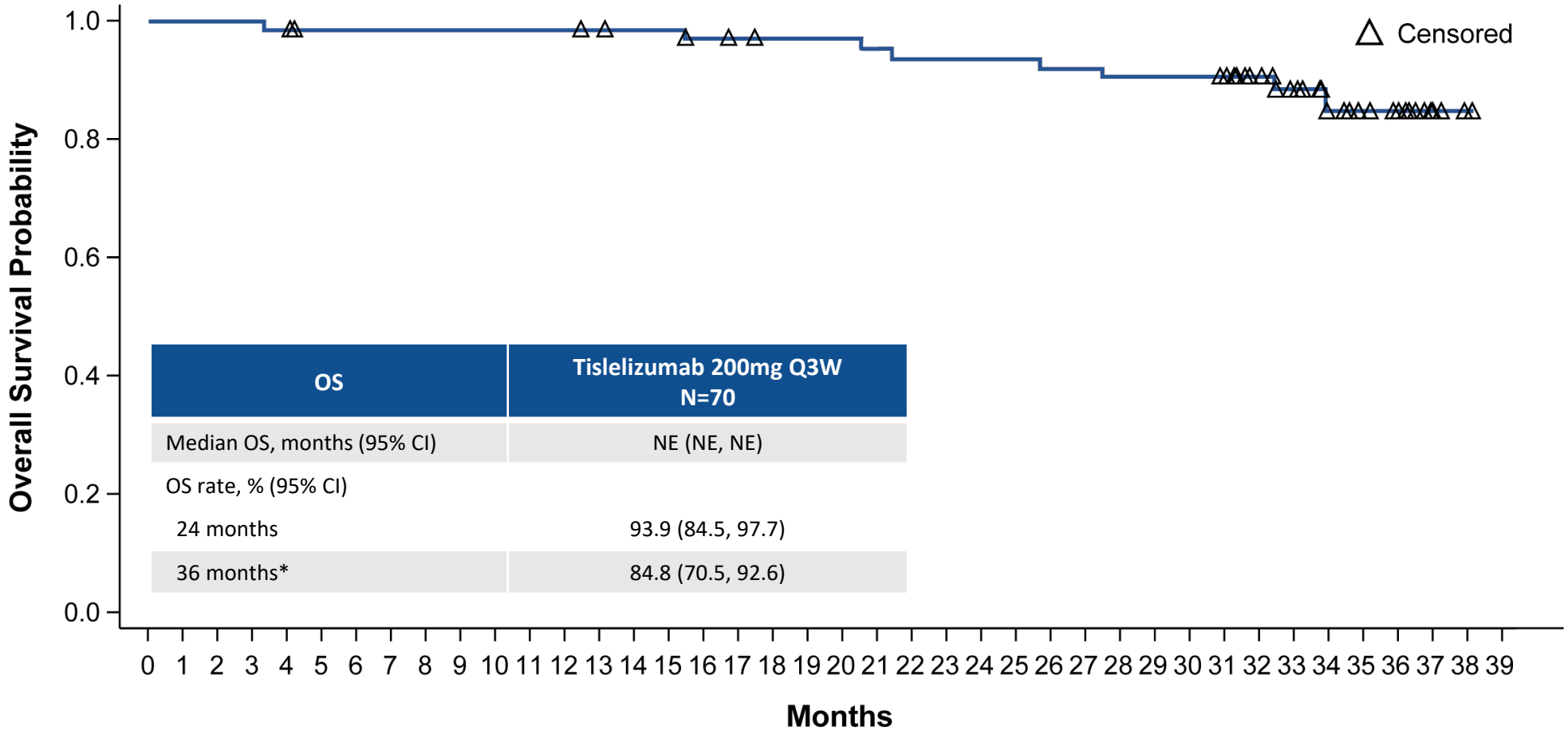
PFS	CR (n=47)	PR+SD (n=16)
Median PFS, months (95% CI)	NE (29.5, NE)	13.2 (5.5, NE)

PFS	Prior ASCT (n=13)	No prior ASCT (n=57)
Median PFS, months (95% CI)	NE (13.2, NE)	27.6 (16.4, NE)

PFS	<3 lines (n=28)	≥3 lines (n=42)
Median PFS months (95% CI)	29.5 (13.0, NE)	34.0 (16.4, NE)

ASCT, autologous hematopoietic stem cell transplant; BOR, best overall response; CR, complete response; No., number; PR, partial response; SD, stable disease; NE, not estimable; PFS, progression-free survival.

OVERALL SURVIVAL



OS	Tislelizumab 200mg Q3W N=70
Median OS, months (95% CI)	NE (NE, NE)
OS rate, % (95% CI)	
24 months	93.9 (84.5, 97.7)
36 months*	84.8 (70.5, 92.6)

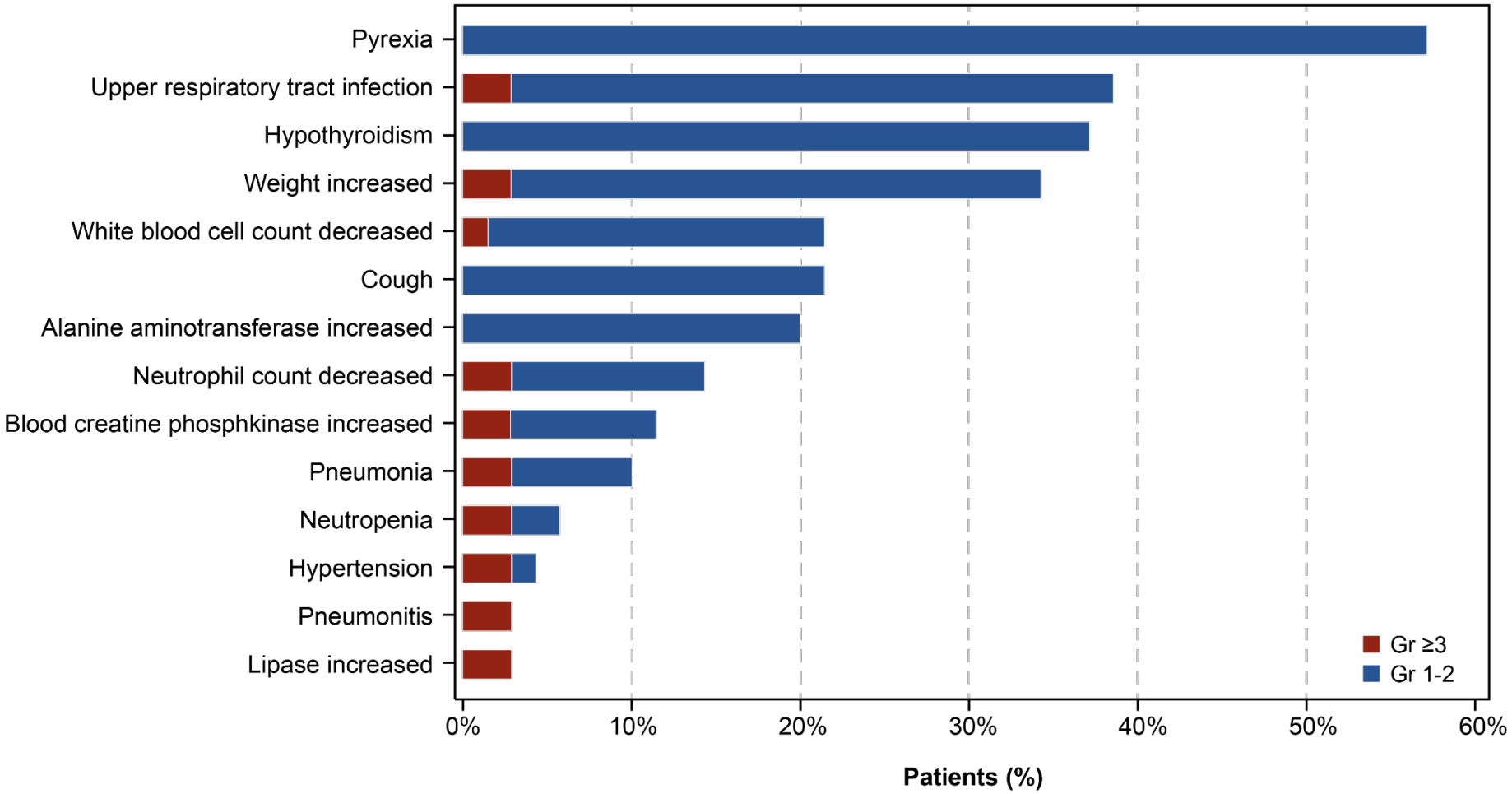
NE, not estimable; No., number; OS, overall survival; Q3W, every 3 weeks.
*Note: Data to be interpreted with caution due to smaller subject number at risk.

SUMMARY OF ADVERSE EVENTS

Event, n (%)	N=70
Patients with at least one TEAE	68 (97.1)
Grade ≥3 TEAE	29 (41.4)
Serious	18 (25.7)
Leading to treatment discontinuation	6 (8.6)
TRAE	68 (97.1)
Grade ≥3 TRAE	22 (31.4)
imAE	32 (45.7)
Most common: hypothyroidism (28.6%), skin adverse reaction (8.6%), pneumonitis (7.1%)	

imAE, immune-mediated adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

FREQUENT TEAEs



TEAEs with all Grades Reported in ≥ 20%, or Grade ≥ 3 Reported in ≥ 2% of Patients

Gr, grade; TEAE, treatment-emergent adverse event.

SUMMARY

- With 33.85 months of extended follow-up, tislelizumab was highly active in R/R cHL patients, as evidenced by:
  - High ORR (87.1%) and CR rate (67.1%) regardless of patient subgroup characteristics
  - Median PFS reached 31.5 months; the estimated 2-year PFS rate was over 55%
- No new safety concerns were identified
- Tislelizumab conferred a favorable benefit versus risk profile and may represent an important treatment option for patients with R/R cHL.

cHL, classical Hodgkin lymphoma; CR, complete response; ORR, overall response rate; PFS, progression-free survival; R/R, relapsed or refractory.

DISCLOSURES

- Dr Song has no competing financial interests to disclose

ACKNOWLEDGMENTS

- We would like to thank the investigators, site support staff, and especially the patients for participating in this study
- This study was sponsored by BeiGene; editorial support was provided by Bio Connections LLC and funded by BeiGene

Thank you