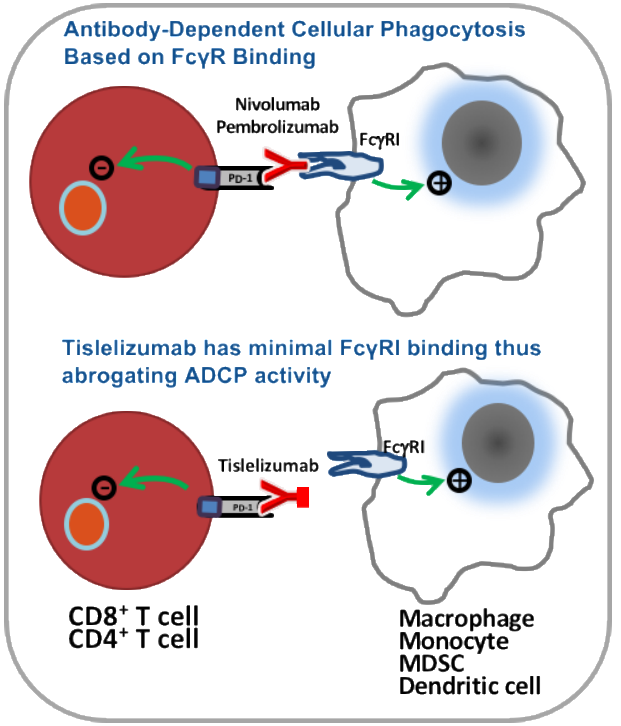
Results of Tislelizumab Monotherapy in Chinese Patients With Relapsed or Refractory Classical Hodgkin Lymphoma:
A Single Arm, Multicenter, Pivotal Phase 2 Study

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

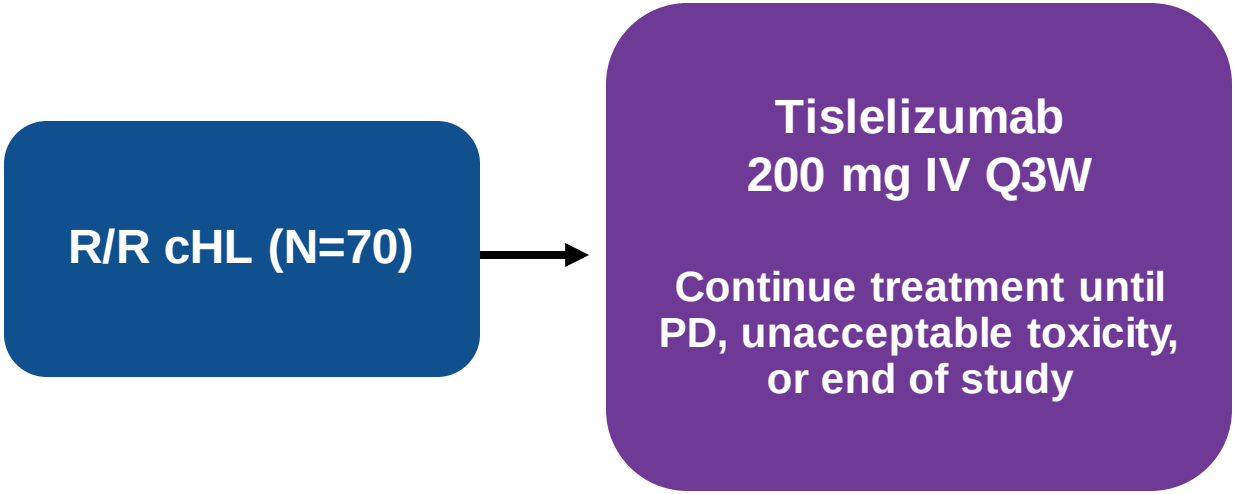
- Patients with relapsed or refractory classical Hodgkin Lymphoma (cHL) who have failed HDT/ASCT, or have chemo-resistant disease and are not candidates for HDT/ASCT, have very poor prognosis
- Anti-PD-1 Abs, including nivolumab and pembrolizumab, are active in this setting. However, only a minority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



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

1. Dahan R. et al. *Cancer Cell*. 2015;28:285-295. 2. Arlauckas S, et al. *Sci Transl Med*. 2017;9(389):eeal3504.

BGB-A317-203: Multicenter, Open-Label, Single-Arm Trial



Primary endpoint:
- ORR assessed by IRC

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

Patients with R/R HL

- 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:

- Response assessments were assessed by IRC using PET-based imaging according to the Lugano Classification (Cheson 2014)

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)
Co-morbidities	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.

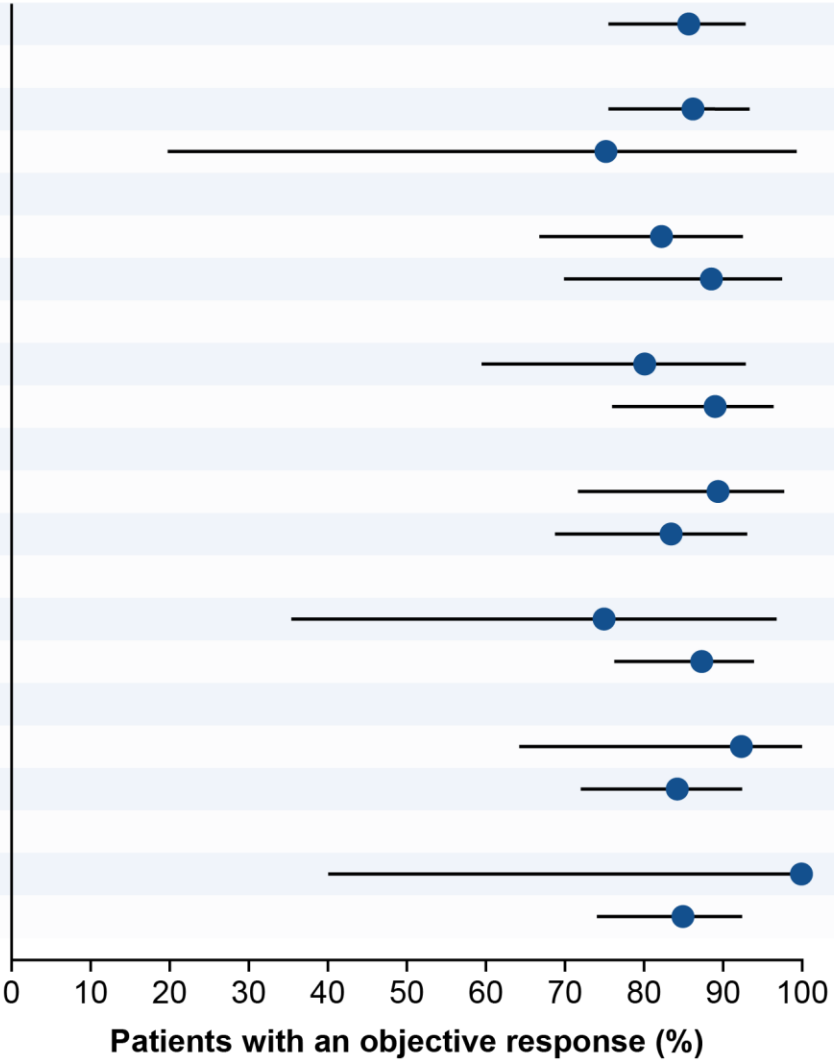
Efficacy: Best overall response by IRC

Best response*, n (%)	N=70
ORR (CR+PR), n (%) [95% CI]†	60 (85.7) [75.3,92.9]
Complete response	43 (61.4)
Partial response	17 (24.3)
Stable disease	4 (5.7)
Progressive disease	5 (7.1)
Died before any postbaseline 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.

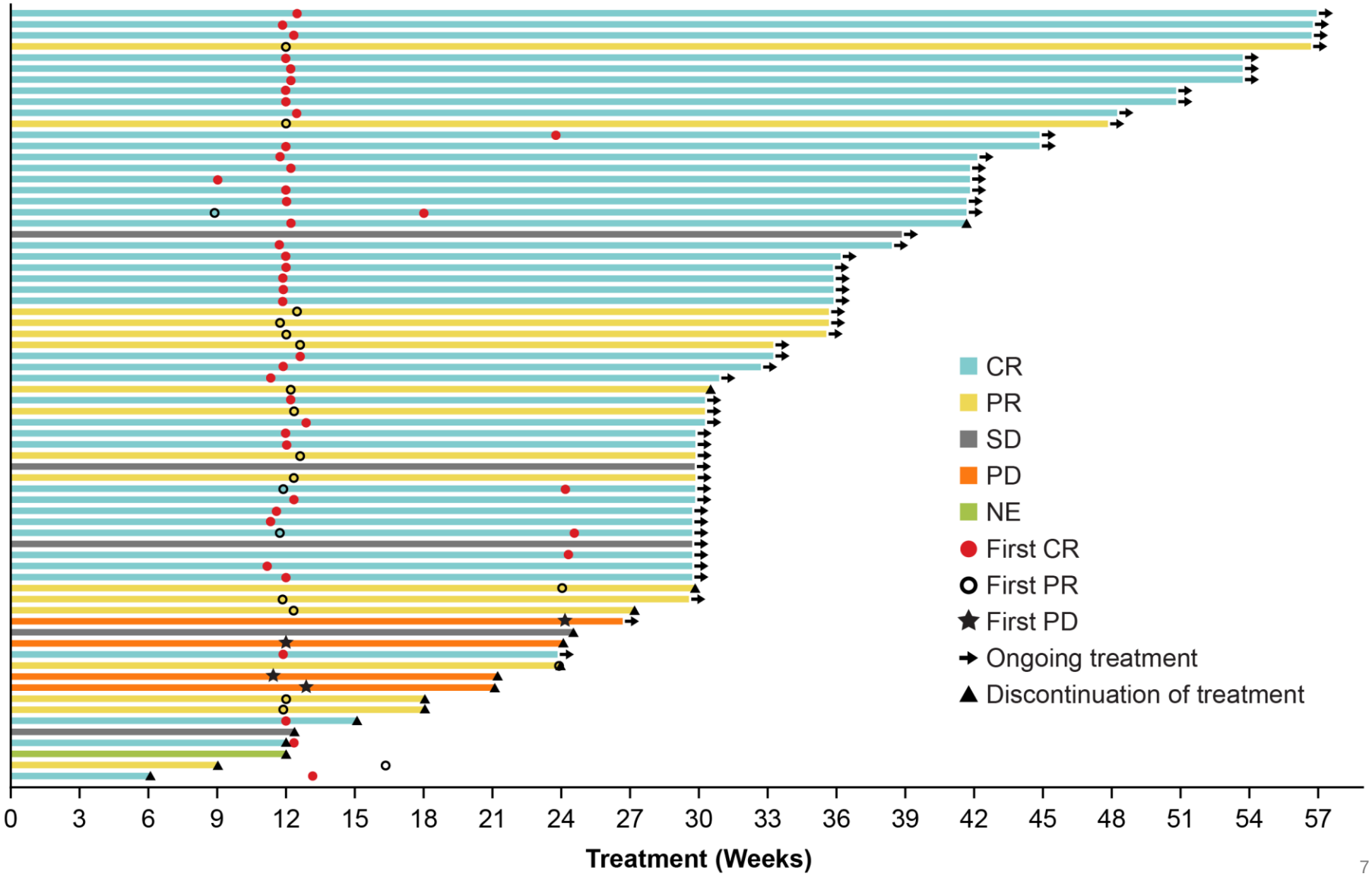
Forest Plot of ORR Based on IRC by Subgroup

Subgroup	Response/Patients	ORR,% (95% CI)*
All patients	60/70	85.7 (75.3, 92.9)
Age group		
Age < 65	57/66	86.4 (75.7, 93.6)
Age ≥ 65	3/4	75.0 (19.4, 99.4)
Sex		
Male	33/40	82.5 (67.2, 92.7)
Female	27/30	90.0 (73.5, 97.9)
Primary refractory		
Yes	20/25	80.0 (59.3, 93.2)
No	40/45	88.9 (75.9, 96.3)
Prior line of therapy for cHL		
< 3	25/28	89.3 (71.8, 97.7)
≥ 3	35/42	83.3 (68.6, 93.0)
Bulky disease		
Yes	6/8	75.0 (34.9, 96.8)
No	54/62	87.1 (76.1, 94.3)
Prior ASCT		
Yes	12/13	92.3 (64.0, 99.8)
No	48/57	84.2 (72.1, 92.5)
Prior Brentuximab		
Yes	4/4	100.0 (39.8, 100.0)
No	56/66	84.8 (73.9, 92.5)

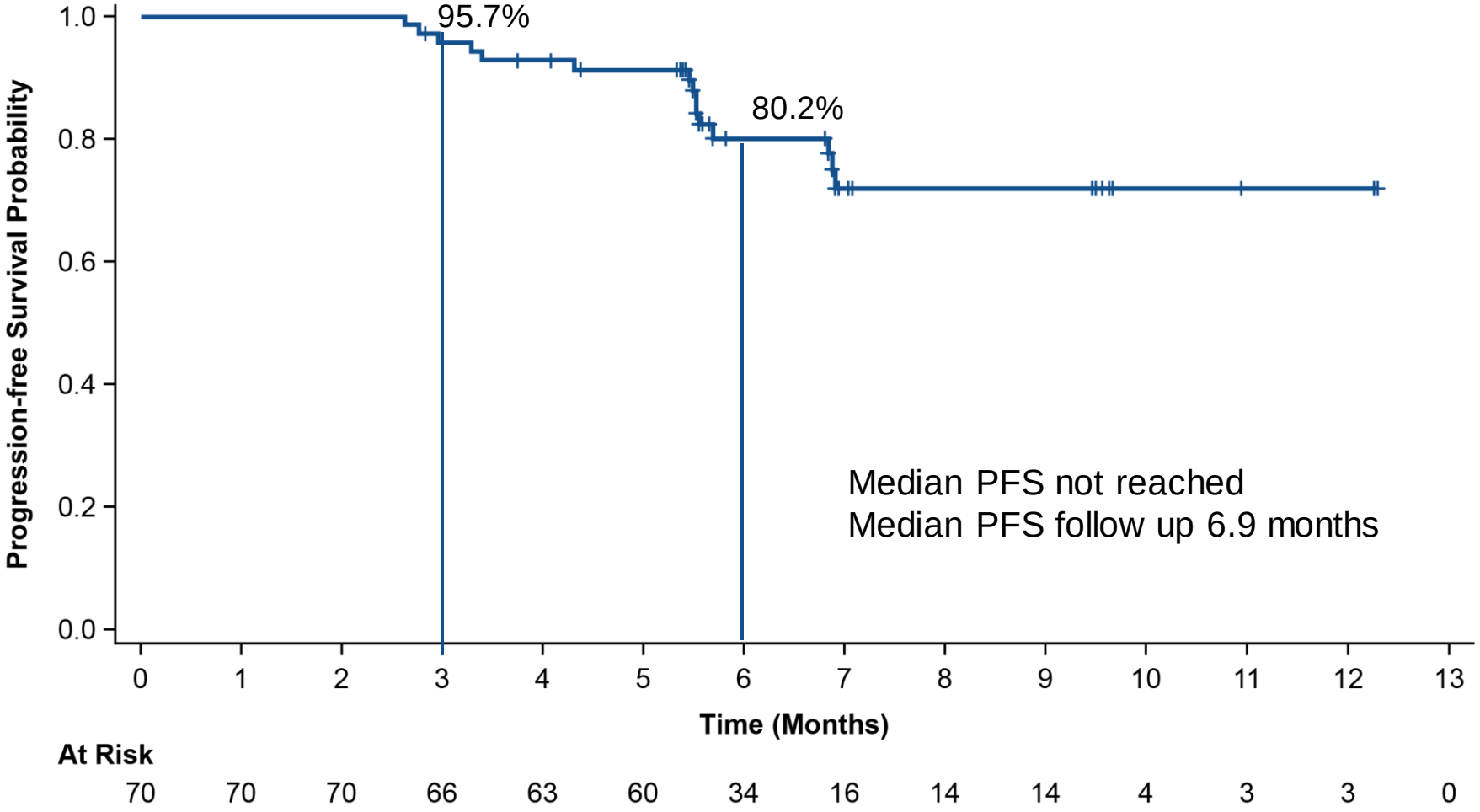


*2-side Clopper-Pearson 95% CIs.

Duration of Treatment and Time to Response



Progression-free Survival



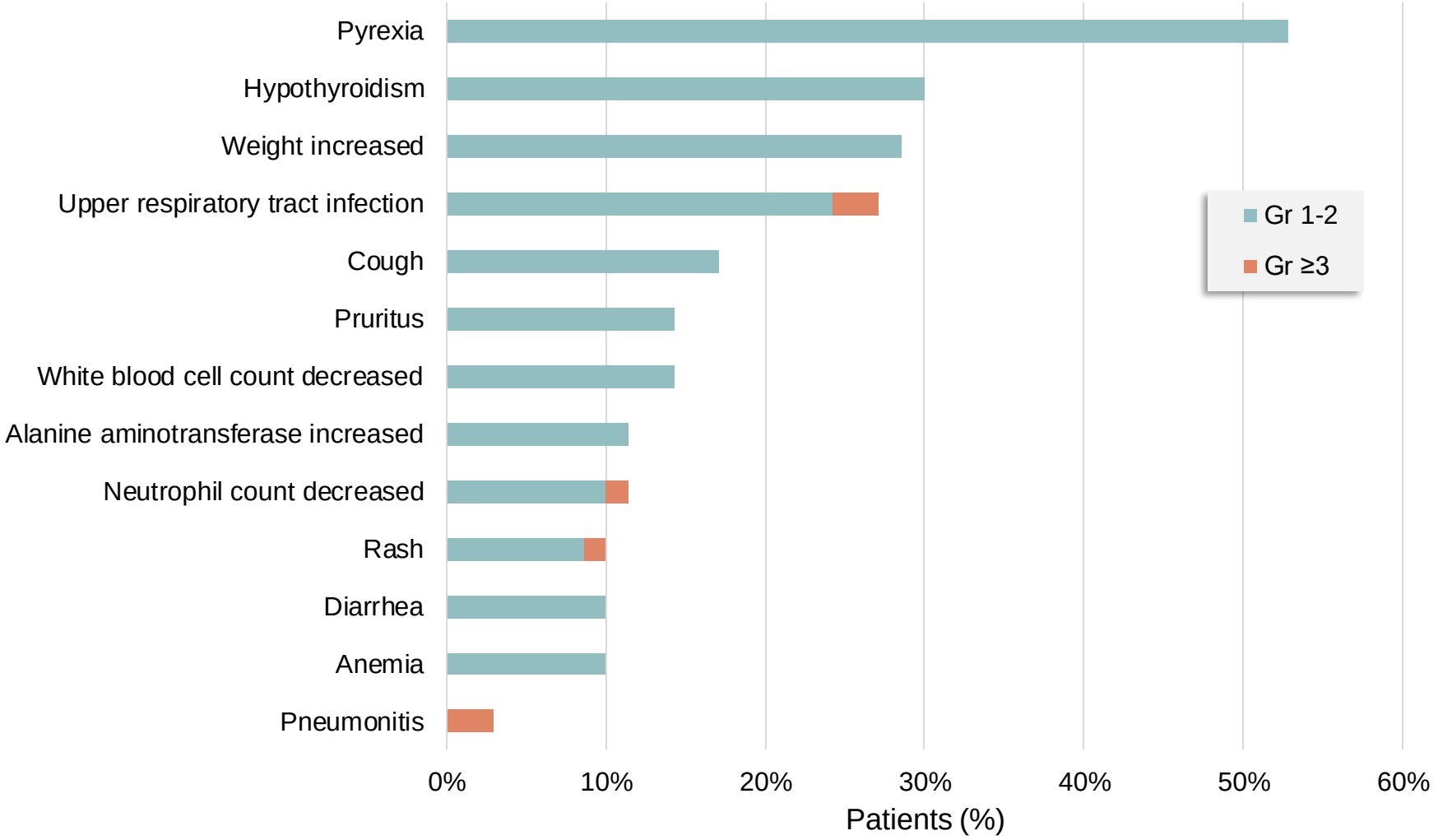
*Kaplan-Meier estimate.

Summary of Treatment-Emergent Adverse Events

Event, n (%)	N=70
Grade ≥3 TEAE	15 (21.4)
Serious TEAE[1]	11* (15.7)
TEAE leading to treatment discontinuation	4† (5.7)
TEAE leading to death	0 (0.0)
Immune-related (ir) TEAEs (by aggregate category)	
≥1 irTEAE	24 (34.3)
Thyroid disorder	13 (18.6)
Pneumonitis	4 (5.7)
Skin adverse reactions	4 (5.7)
Musculoskeletal‡	2 (2.9)
Hepatitis	1 (1.4)
Nephritis and renal dysfunction	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, osteoarthritis

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



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

Summary

- 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-PD1 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 rate of CR (86% and 61%, respectively)
  - Median duration of response not reached

Acknowledgements

- 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