

# Tislelizumab, an Anti-PD-1 Antibody, in Patients With Relapsed/Refractory Classical Hodgkin Lymphoma in TIRHOL BGB-A317-210: A Prospective Multicenter LYSA Phase 2 Study Conducted in Western Countries



Hervé Ghesquière,<sup>1</sup> Krime Bouabdallah,<sup>2</sup> Marc André,<sup>3</sup> Philippe Quittet,<sup>4</sup> Cécile Borel,<sup>5</sup> Aspasia Stamatoullas Bastard,<sup>6</sup> Michael Gilbertson,<sup>7</sup> Fabien Le Bras,<sup>8</sup> Catherine Thieblemont,<sup>9</sup> Baptiste Delapierre,<sup>10</sup> Mohamed Touati,<sup>11</sup> Pierre Feugier,<sup>12</sup> Julien Lazarovici,<sup>13</sup> Nadine Morineau,<sup>14</sup> Thomas Gastinne,<sup>15</sup> Isabelle Chaillol,<sup>16</sup> Rod Ramchandren,<sup>17</sup> Harsh Shah,<sup>18</sup> Dipenkumar Modi,<sup>19</sup> Heather Allewelt,<sup>20</sup> Pierre Fustier,<sup>21</sup> Jianfeng Xu,<sup>20</sup> Amit Agarwal,<sup>20</sup> Franck Morschhauser,<sup>22</sup> Cédric Rossi<sup>23</sup>

<sup>1</sup>Lyon Sud Hospital, Pierre Benite, France; <sup>2</sup>CHU Bordeaux Pessac, Bordeaux, France; <sup>3</sup>CHU UCL Namur, Yvoir, Belgium; <sup>4</sup>CHU Montpellier, Montpellier, France; <sup>5</sup>IUCT Oncopole, Toulouse, France; <sup>6</sup>Centre Henri Becquerel, Rouen, France; <sup>7</sup>Monash Health, Melbourne, Australia; <sup>8</sup>CHU Mondor, Creteil, France; <sup>9</sup>Hopital Saint-Louis, Paris, France; <sup>10</sup>Caen University Hospital, Caen, France; <sup>11</sup>CHU Limoges, Limoges, France; <sup>12</sup>CHU Nancy, Nancy, France; <sup>13</sup>Gustave Roussy Institute, Villejuif, France; <sup>14</sup>CHD de Vendee, La Roche Sur Yon, France; <sup>15</sup>CHU de Nantes, Nantes, France; <sup>16</sup>Lymphoma Academic Research Organisation, Lyon, France; <sup>17</sup>University of Tennessee Medical Center, Knoxville, TN, USA; <sup>18</sup>University of Utah, Salt Lake City, UT, USA; <sup>19</sup>Karmanos Cancer Institute, Detroit, MI, USA; <sup>20</sup>BeiGene, San Mateo, CA, USA; <sup>21</sup>BeiGene, Basel, Switzerland; <sup>22</sup>CHU de Lille, Lille, France; <sup>23</sup>CHU Dijon, Dijon, France

## BACKGROUND

- Programmed cell death protein-1 (PD-1) blockade is commonly used to treat relapsed/refractory (RR) classical Hodgkin lymphoma (cHL), but the overall response rates (ORRs) and complete response rates (CRRs) of approved anti-PD-1 antibodies remain suboptimal
- Tislelizumab blocks PD-1 with a high specificity and affinity, and minimized FcγR binding on macrophages leads to reduced clearance<sup>1</sup>
- Results of the initial phase 2 study of tislelizumab in Chinese patients with RR cHL were impressive, with an ORR and a CRR of 87% and 63%, respectively, and 3-year progression-free survival (PFS) of 40%<sup>2,3</sup>
- These results need further evaluation in a broader population with different standards of care, including more frequent use of autologous stem cell transplantation (ASCT) and targeted agents

## METHODS

### Inclusion Criteria

- TIRHOL (NCT04318080) is an international, prospective, phase 2 study for patients with RR cHL, conducted in France, Belgium, the USA, and Australia
- Histologically confirmed cHL
- Patients must have relapsed or refractory cHL
- Eastern Cooperative Oncology Group performance status of 0 or 1
- Measurable disease defined as ≥1 F-fluorodeoxyglucose-avid lesion
- Cohort 1 included patients who previously underwent ASCT
- Cohort 2 included patients who were ineligible for ASCT
- Prior therapy with brentuximab vedotin was required in initial design
  - The protocol was amended to remove this criterion for both cohorts in October 2021

### Statistics

- The primary endpoint was ORR (best overall response of complete response [CR] or partial response), as assessed by investigator, according to positron emission tomography-computed tomography (PET-CT) International Lugano 2014 criteria
- Null hypothesis is ORR=45%, based on previous clinical trials, and alternative hypothesis is ORR >45%
- Assuming an alternative ORR of 65% compared with the null ORR of 45% in cohort 1 and cohort 2 combined, using a binomial exact test, the power to reject the null hypothesis with 42 patients at a one-sided alpha of 0.05 is greater than 80%
- Secondary endpoints were the CRR, time to response, duration of response, and safety and tolerability of tislelizumab
- PFS and overall survival were the main exploratory endpoints

### Study Design

- From August 2020 to September 2022, 45 patients were enrolled and dosed
  - Cohort 1, N=14
  - Cohort 2, N=31
- Tislelizumab 200 mg was given intravenously every 3 weeks until progressive disease (PD), unacceptable toxicity, or study withdrawal
- Tumor assessments were performed every 12 weeks by PET-CT
- The data cut-off date for this primary analysis was December 12, 2022

## RESULTS

**Table 1. Clinical Characteristics**

	Cohort 1 N=14	Cohort 2 N=31	Total N=45
Age (years)			
Median (range)	49 (24–69)	69 (18–87)	64 (18–87)
≥45 years, n (%)	8 (57)	23 (74)	31 (69)
Sex			
Male	10 (71)	20 (65)	30 (67)
Female	4 (29)	11 (35)	15 (33)
Time since initial diagnosis, months			
N	11	28	39
Median (range)	40.2 (22–229)	14.1 (6–326)	24.7 (6–326)
Pathological diagnosis, n (%)			
Nodular sclerosis cHL	5 (36)	13 (42)	18 (40)
cHL + unclassified	4 (29)	13 (42)	17 (38)
Lymphocyte-rich cHL	2 (14)	1 (3)	3 (7)
Mixed cellularity cHL	0 (0)	1 (3)	1 (2)
Insufficient material for review	3 (21)	3 (10)	6 (13)
Patient status at time of enrollment, n (%)			
Refractory	0 (0)	13 (42)	13 (29)
Relapse/progression	14 (100)	18 (58)	32 (71)
Ann Arbor stage, n (%)			
II	4 (29)	5 (16)	9 (20)
III	5 (36)	12 (39)	17 (38)
IV	5 (36)	14 (45)	19 (42)
Performance status (ECOG), n (%)			
0	10 (71)	18 (58)	28 (62)
1	4 (29)	13 (42)	19 (38)
B symptoms, Yes, n (%)	3 (21)	5 (16)	8 (18)
International prognostic score, n (%)			
0–2	9 (64)	13 (43)	22 (50)
≥3	5 (36)	17 (57)	22 (50)
Missing	0	1	1
Bulky disease, Yes, n (%)	3 (21)	2 (7)	5 (11)
Number of prior lines of therapy for cHL, n (%)			
1	0 (0)	7 (23)	7 (16)
2	9 (64)	17 (55)	26 (58)
3	4 (29)	6 (19)	10 (22)
4	1 (7)	1 (3)	2 (4)
Median (range)	2 (2–4)	2 (1–4)	2 (1–4)
Prior therapies for cHL, n (%)			
Monoclonal antibody <sup>a</sup>	11 (79)	23 (74)	34 (76)
Chemotherapy	14 (100)	31 (100)	45 (100)
Radiotherapy	6 (43)	4 (13)	10 (22)
Autologous transplant	14 (100)	0 (0)	14 (31)
Other anticancer therapy	0 (0)	2 (7)	2 (4)

<sup>a</sup>33 (73%) received prior BV. cHL, classical Hodgkin lymphoma; ECOG, Eastern Cooperative Oncology Group.

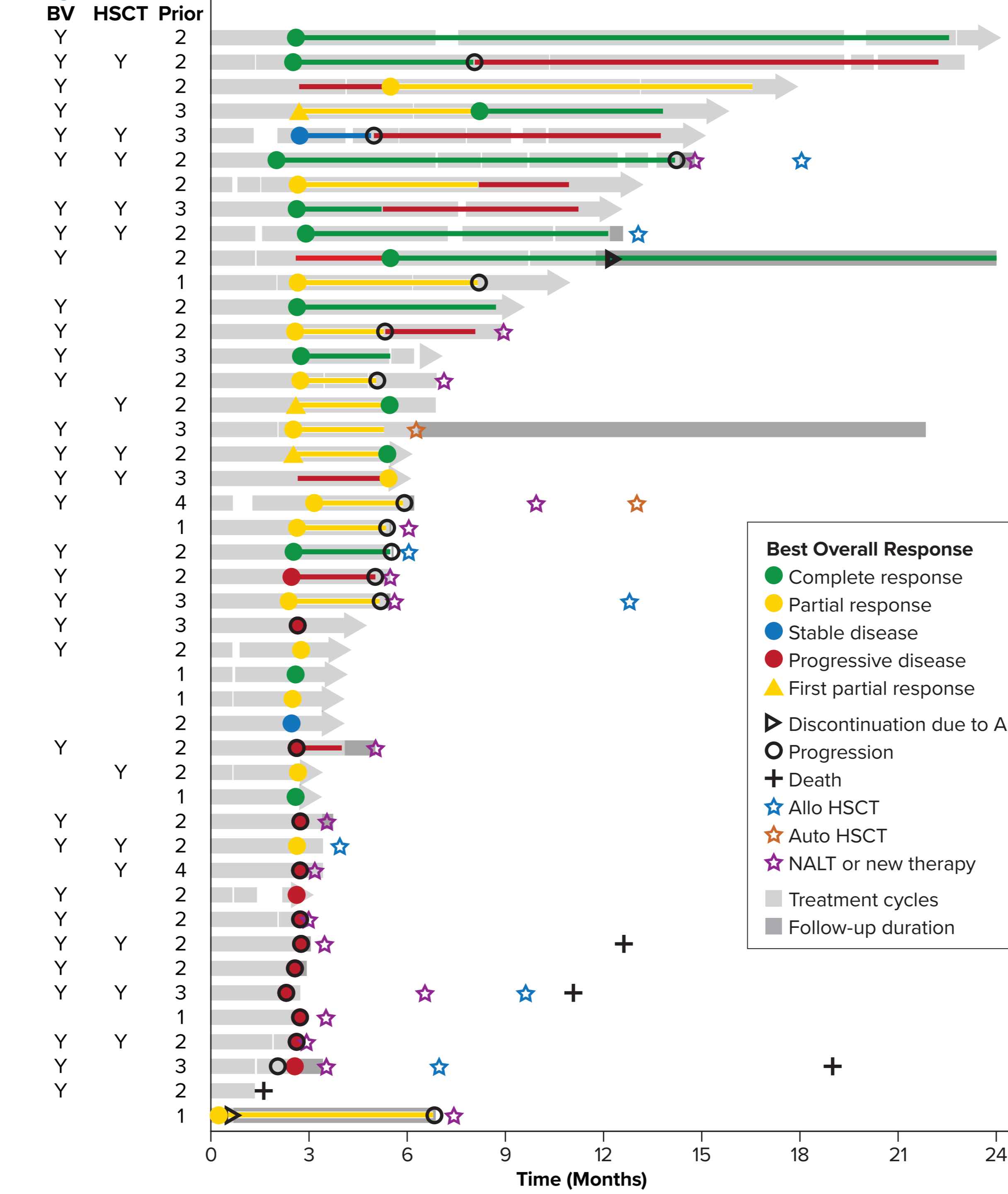
**Table 2. Response to Treatment**

	N=45
Best response according to Lugano classification, n (%)	
Complete remission	14 (31.1)
Partial remission	15 (33.3)
Stable disease	2 (4.4)
Progressive disease	13 (28.9)
Not evaluated	1 (2.2)
ORR according to Lugano classification, n (%)	29 (64.4)
90% CI for ORR rate	51.1–76.3
Binomial test for analyses of primary endpoint	
Z test value	2.62
One-sided P value	.0044

CI, confidence interval; ORR, overall response rate.

- ORR in cohort 1 was 64.3% (n=9/14) and in cohort 2 was 64.5% (n=20/31)
- Median number of tislelizumab doses (cycles) was 8 (range, 1–33)
- Median duration of treatment was 24 weeks (range, 3–105)
- Three patients with objective response underwent subsequent ASCT (1) or allogeneic SCT (2)

**Figure 1. Swimmer Plot for Response**



- As of the data cut-off date of December 12, 2022:
  - 19 patients remain on tislelizumab
  - 11 (24%) have continued treatment for >1 year
- 13 patients with SUV increase meeting PD criteria but continued clinical benefit continued tislelizumab for a median of 3.6 months (range Q1: 1.8–Q3: 9.5) after PD

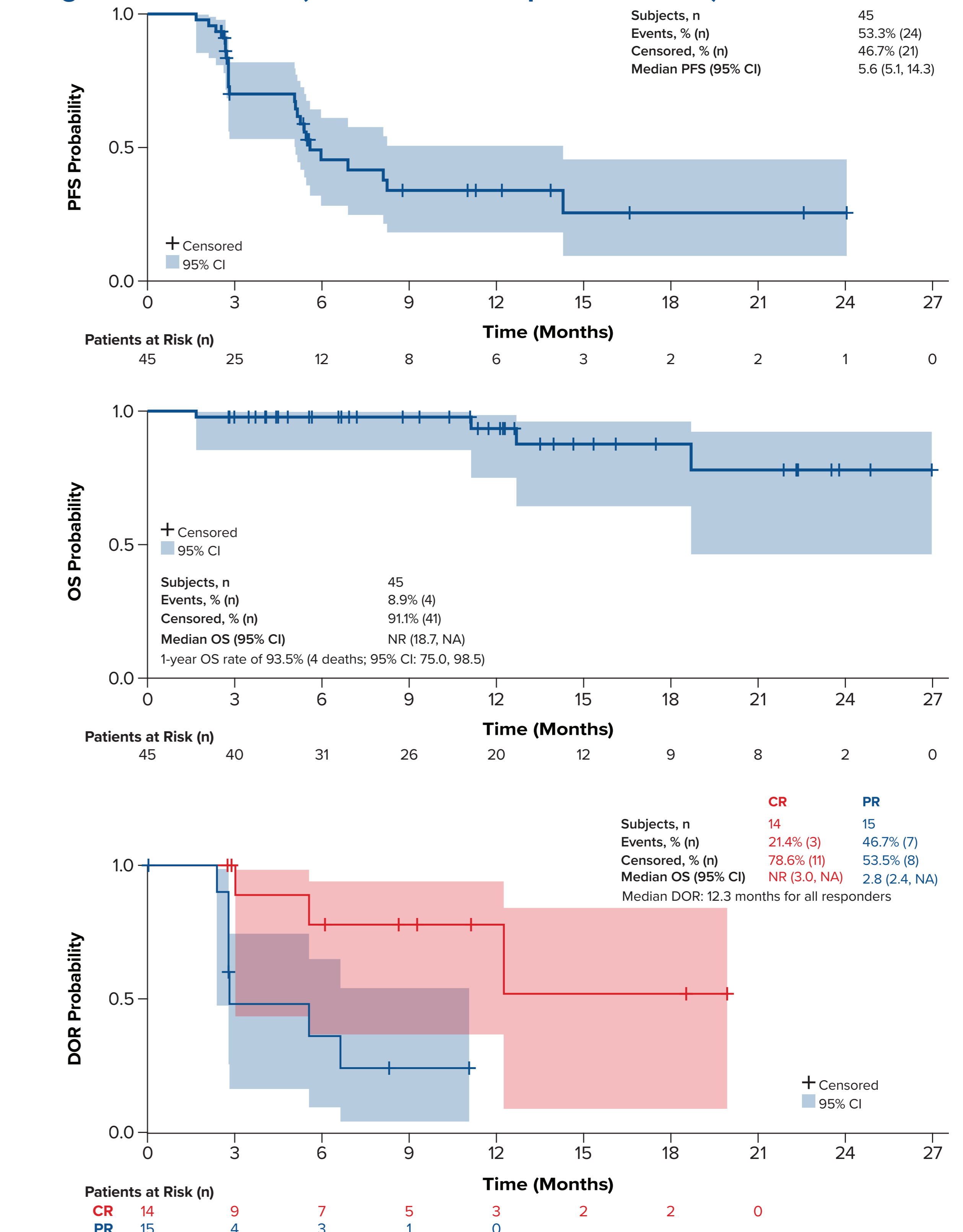
### Toxicity

- No treatment-emergent AEs leading to death
- Grade ≥3 treatment-emergent AEs: 15 (33%) patients
- Discontinuation (n=9) or interruption (n=2) of tislelizumab
- Immune-related (ir) AEs: 15 (33%) patients
  - Three patients had grade ≥3 irAEs: maculopapular rash, hepatitis, hemolytic anemia (n=1 each)

## CONCLUSIONS

- TIRHOL met its primary endpoint, with an ORR of 64% (90% CI, 51.1–76.3) and a CRR of 31%, and with an acceptable safety profile
  - ORR was similar in cohort 1 (n=9/14, 64.3%) and cohort 2 (n=20/31, 64.5%)
- This study confirmed that tislelizumab is a promising treatment option in cHL
  - The A317-210 study population was much older than in prior studies<sup>2,3</sup> suggesting that tislelizumab is an attractive treatment option for older patients with cHL
- Study follow-up is ongoing, but durable responses have been observed, especially in patients achieving CR

**Figure 2. Outcomes (Median Follow-Up: 11.4 Months)**



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