

Five-year overall survival from the CheckMate 205 study of nivolumab for relapsed or refractory classical Hodgkin lymphoma

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Introduction

- Programmed death-1 (PD-1) immune checkpoint inhibitors, including nivolumab, have shown strong activity in patients with relapsed/refractory (R/R) classical Hodgkin lymphoma (cHL).^{1,2}
 - In the CheckMate 205 study (NCT02181738) at a median follow-up of 33 months, the overall response rate (ORR) was 71% (95% CI, 65-77), duration of response (DOR) was 18 months (95% CI, 13-25) and progression-free survival (PFS) was 15 months (95% CI, 11-19) in patients with R/R cHL after autologous hematopoietic cell transplantation (auto-HCT).⁴
- In a recent phase 3 randomized trial, PD-1 inhibitor monotherapy showed significantly improved PFS vs brentuximab vedotin (BV) in patients with R/R cHL.²
- The long-term survival benefit of anti-PD-1 therapy and optimal duration of treatment in patients with R/R cHL remain unknown

Objective

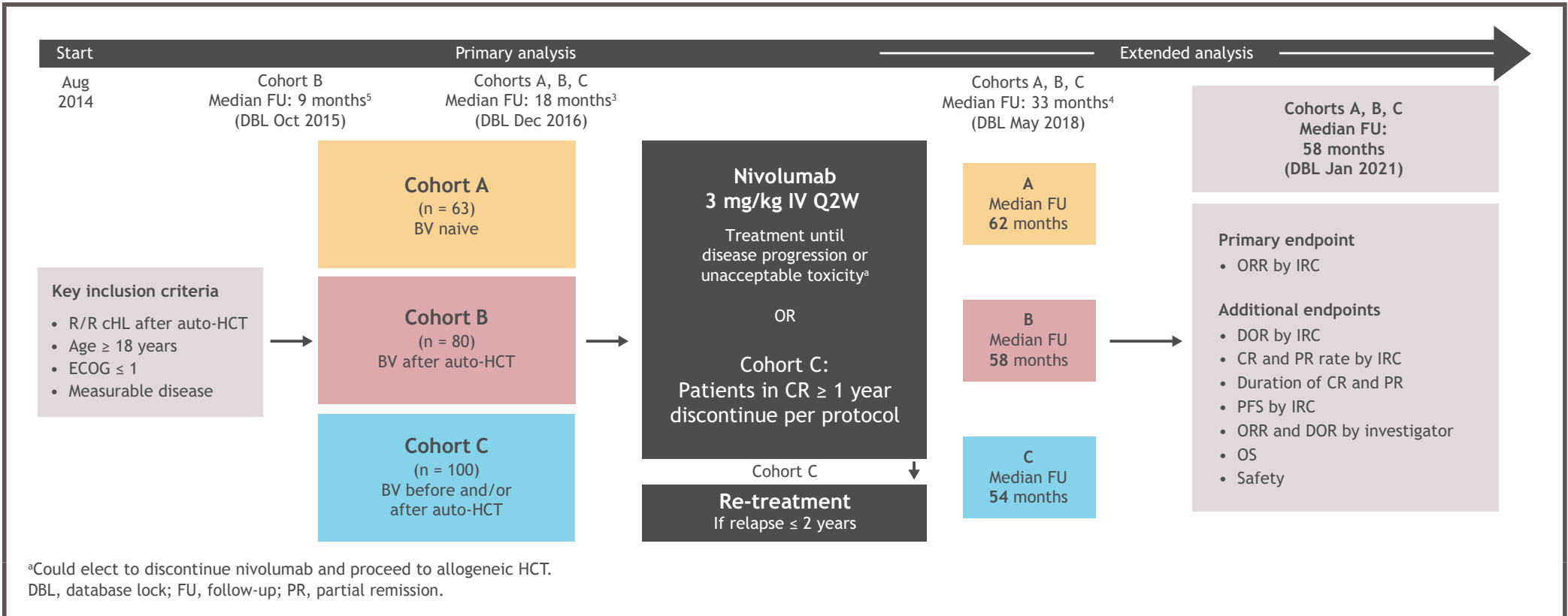
- To assess the longer-term outcomes of CheckMate 205 with a median follow-up of 58 months

Methods

Study design

- Patients who progressed or relapsed after auto-HCT were enrolled in CheckMate 205 into 3 independent cohorts based on previous treatment (Figure 1)
- Patients in cohort C who had complete remission (CR) for ≥ 1 year discontinued treatment per protocol with the option of re-treatment if relapse occurred within 2 years
- The primary endpoint was ORR per independent review committee (IRC); additional endpoints included DOR, PFS, overall survival (OS), and safety

Figure 1. CheckMate 205 study design



Results

Baseline characteristics

- Among the 243 patients enrolled, 42% were female and the median age of patients was 34 years (range, 18-72) (Table 1)
- At study entry, 57% had stage IV disease and 22% had B symptoms
- The median number (interquartile range [IQR]) of prior lines of therapy overall was 4 (3-5)

Table 1. Baseline demographics and clinical characteristics

Characteristic	Cohort A n = 63	Cohort B n = 80	Cohort C n = 100	Overall N = 243
Age, median (range), years	33 (18-65)	37 (18-72)	32 (19-69)	34 (18-72)
Female, %	46	36	44	42
Stage IV disease,* %	38	68	61	57
B symptoms,* %	16	23	25	22
Bulky disease,* %	16	21	22	20
Extralymphatic involvement, %	38	45	45	43
Prior lines of therapy, median (IQR) [‡]	2 (2-3)	4 (4-7)	4 (3-5)	4 (3-5)
Time from diagnosis to first dose of nivolumab, median (IQR), years [‡]	3.1 (2.0-7.5)	6.2 (3.3-8.3)	3.5 (2.3-6.4)	4.5 (4.5-7.6)

*At study entry.

Patient disposition

- At the data cutoff, 8% of patients were still on treatment (Table 2)
- The most common reasons for discontinuation were progressive disease (40%), study drug toxicity (10%), and patient request to discontinue (9%)
- Overall, 24% of patients subsequently received auto-HCT

Table 2. Patient disposition after extended follow-up

Disposition	Cohort A n = 63	Cohort B n = 80	Cohort C n = 100	Overall N = 243
Patients still on treatment, n (%)	10 (16)	6 (8)	3 (3)	19 (8)
Reason off treatment, %				
Progressive disease	40	43	38	40
Study drug toxicity	10	14	8	10
Patient request to discontinue	8	15	5	9
AEs unrelated to study drug	5	4	1	3
Maximum clinical benefit	3	0	1	1
Completed treatment	0	0	13 ^a	5
Other	19	18	31	23
Duration of treatment, median (95% CI), months	18 (12-23)	16 (9-24)	14 (11-15)	14 (13-16)
Duration of treatment after progression, median (95% CI), months ^b	4 (2-11)	6 (3-13)	4 (3-9)	5 (3-8)
Subsequent HCT,* %	22	18	30	24

^aIncludes 12 patients in Cohort C who had persistent CR for ≥ 1 year and discontinued per protocol; ^bn = 23, 30, 34, and 87 for Cohorts A, B, C, and overall, respectively; ^cPatients may have discontinued for additional reasons and subsequently received allogeneic HCT (except 1 patient in Cohort A who received auto-HCT); AE, adverse event.

Safety

- Treatment-related adverse events (TRAEs) occurred in 82% of patients (28% had grade 3/4) (Table 3)
 - The most common (≥ 10% of patients) TRAEs of any grade were fatigue (25%), diarrhea (16%), infusion-related reaction (14%), rash (12%), nausea (11%), pruritus (10%), and pyrexia (10%); almost all were grade 1/2
- Treatment-related serious AEs of any grade occurred in 15% of patients (9% had grade 3/4) (Table 3)
 - The most common treatment-related serious AEs of any grade were pneumonitis and infusion-related reactions (2% each)
- Overall, 11% of patients had TRAEs of any grade leading to discontinuation; the most common TRAEs of any grade leading to discontinuation were pneumonitis (3%), autoimmune hepatitis (2%), diarrhea (1%), and increased aspartate aminotransferase (1%)
- There were no deaths due to TRAEs
- The most common immune-mediated AEs of any grade were rash (12%), hepatitis (6%), and pneumonitis (6%) (Table 4)

Table 3. Serious AEs and AEs leading to discontinuation

TRAEs, n (%)	Overall population N = 243	
	Any grade	Grade 3/4
Patients with TRAEs	200 (82)	68 (28)
Patients with treatment-related serious AEs	36 (15)	22 (9)
≥ 1% of patients		
Pneumonitis	6 (2)	3 (1)
Infusion-related reaction	5 (2)	1 (< 1)
Pleural effusion	2 (1)	0
Colitis	2 (1)	2 (1)
Diarrhea	2 (1)	2 (1)
Pneumonia	2 (1)	2 (1)
Pyrexia	2 (1)	0
Autoimmune hepatitis	2 (1)	2 (1)
Patients with TRAEs leading to discontinuation	26 (11)	16 (7)
≥ 1% of patients		
Pneumonitis	8 (3)	2 (1)
Autoimmune hepatitis	4 (2)	4 (2)
Diarrhea	2 (1)	1 (< 1)
Aspartate aminotransferase increased	2 (1)	2 (1)

Table 4. Immune-mediated AEs

Patients with immune-mediated AEs, n (%)	Overall population N = 243	
	Any grade	Grade 3/4
Rash	29 (12)	4 (2)
Hepatitis	15 (6)	12 (5)
Pneumonitis	15 (6)	2 (1)
Hypersensitivity	13 (5)	2 (1)
Diarrhea/colitis	6 (2)	5 (2)
Nephritis/renal dysfunction	3 (1)	1 (< 1)
Adrenal insufficiency	1 (< 1)	0
Hyperthyroidism	1 (< 1)	0

Efficacy

- The ORR was 71% (95% CI, 65-77)
 - The CR rate increased from 16% at 18 months of follow-up to 21% at 58 months of follow-up (Table 5)
- In all responders, the median DOR was 18.2 months (95% CI, 14.7-26.1) (Figure 2)
- Overall, the 2-year and 5-year PFS rates were 37% (95% CI, 30-44) and 18% (95% CI, 12-25), respectively (Figure 3)
 - Patients who achieved CR had longer median PFS (37.4 months) and DOR (30.3 months) than patients who achieved PR (15.2 and 13.5 months, respectively) (Figure 2-3)

Table 5. BOR after extended follow-up

Response	Cohort A n = 63	Cohort B n = 80	Cohort C n = 100	Overall N = 243
ORR, % (95% CI)	65 (52-77)	71 (60-81)	75 (65-83)	71 (65-77)
BOR,* %				
CR	32	14	21	21
PR	33	58	54	50
SD	22	18	12	17
PD	13	9	11	11
Time to response, median (IQR), months				
Any response	2.0 (1.9-2.3)	2.2 (1.9-3.0)	2.1 (1.9-3.8)	2.1 (1.9-3.6)
CR	3.9 (3.7-5.2)	4.4 (3.7-19.1)	4.2 (3.7-6.5)	4.0 (3.7-8.3)

Numbers may not sum to 100% due to rounding.
^aResponse could not be determined in 4 patients (no post-baseline scan available, n = 3; post-baseline scans unknown, n = 1).
BOR, best overall response; PD, progressive disease; SD, stable disease.

Figure 2. DOR by BOR

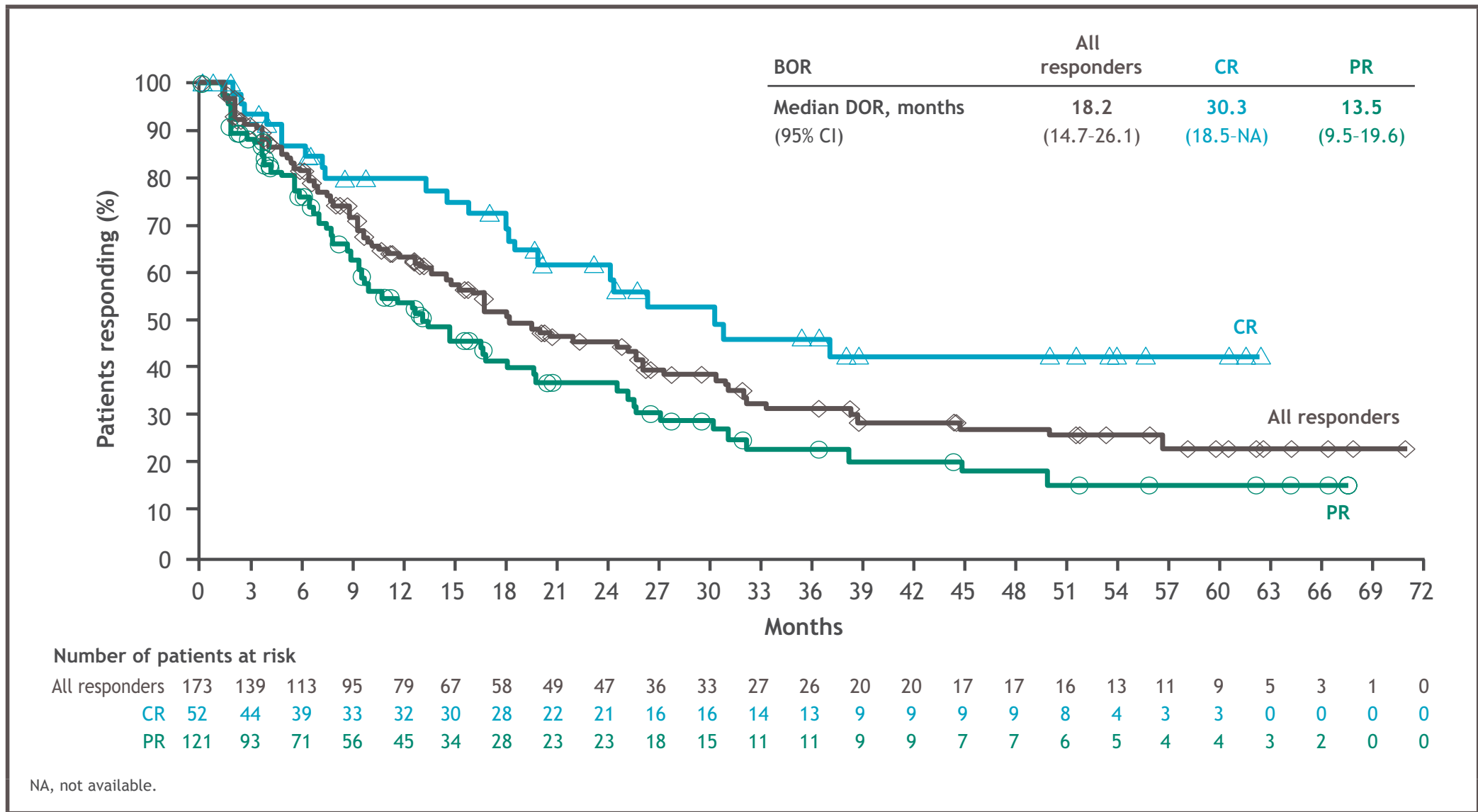
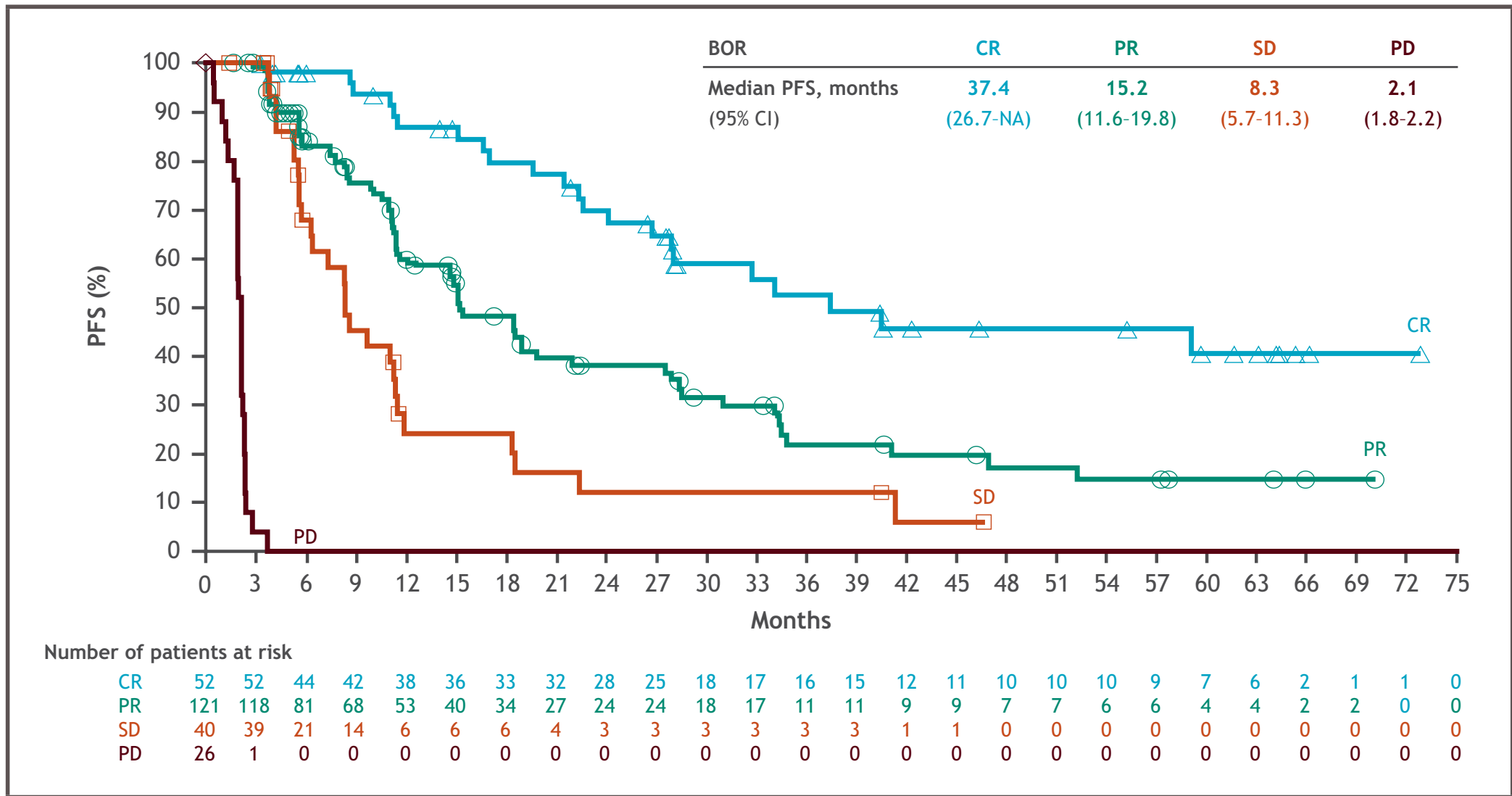


Figure 3. PFS by BOR



- The 2-year and 5-year OS rates were 87.1% (95% CI, 82.0-90.8) and 71.4% (95% CI, 64.8-77.1), respectively (Figure 4)
 - Patients who achieved CR also had improved OS versus patients with PR
- In this extended analysis, responses remained durable (Table 6)

Figure 4. OS by BOR

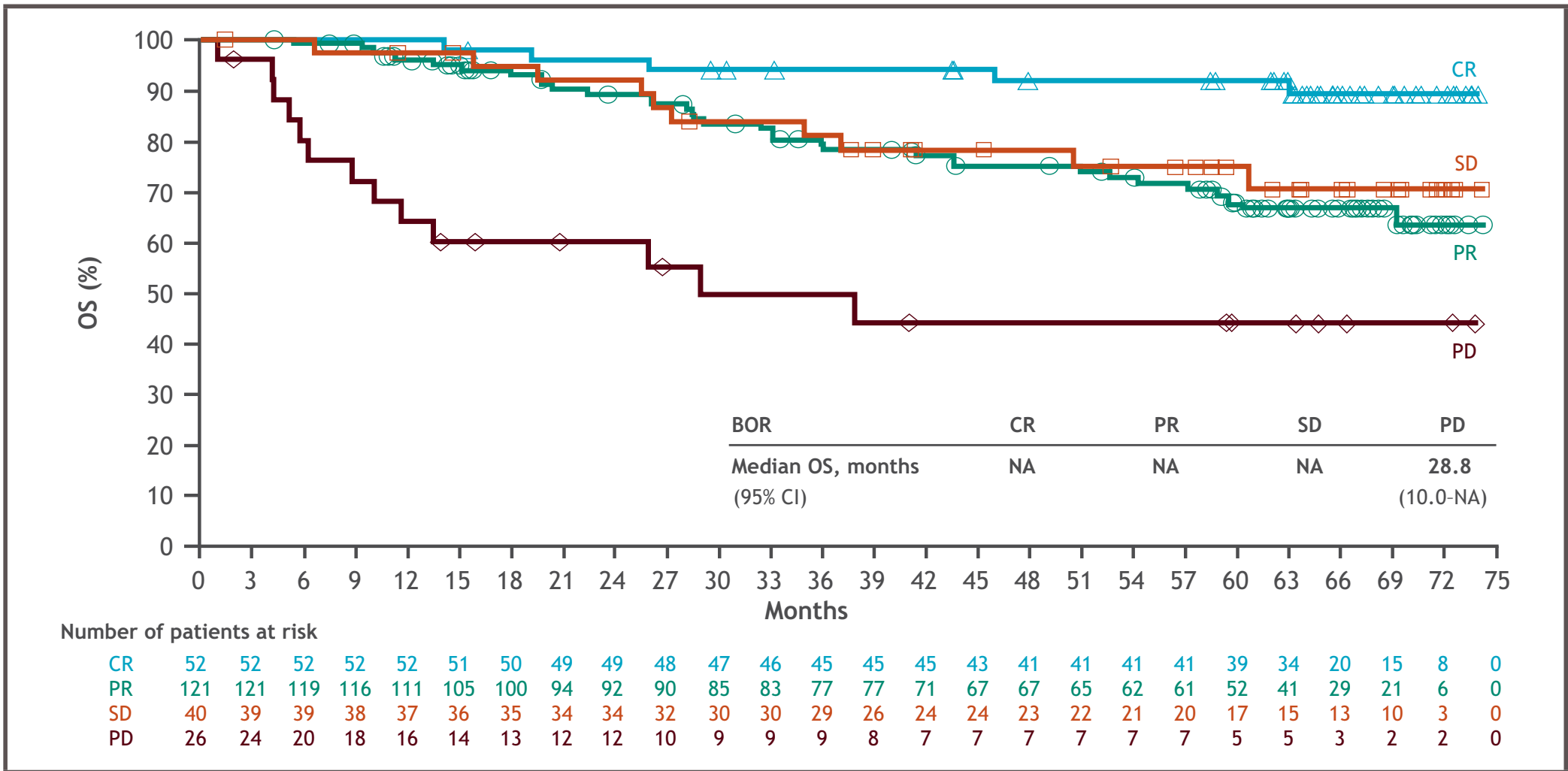


Table 6. Response rates over time

Endpoint	Median duration of follow-up		
	18 months [‡]	33 months [‡]	58 months
ORR, % (95% CI)	69 (63-75)	71 (65-77)	71 (65-77)
CR, %	16	21	21
DOR, median (95% CI), months	16.6 (13.2-20.3)	18 (13.5-25.3)	18.2 (14.7-26.1)
PFS, median (95% CI), months	14.7 (11.3-18.5)	15 (11-19)	15.1 (11.3-18.5)

Cohort C patients

- There were 12 patients from cohort C who discontinued study treatment after ≥ 1 year of persistent CR
- At the time of analysis, 6 patients had completed the observational follow-up period
- Among the 6 patients who did not complete the observational follow-up period, 4 patients had disease progression
 - 1 patient received commercial nivolumab off-study
 - 3 were re-treated per protocol with nivolumab (2 re-achieved CR and 1 achieved PR)

Conclusions

- This 5-year follow-up of CheckMate 205 Cohorts ABC confirms the efficacy and safety of nivolumab for patients with cHL who progressed or relapsed after auto-HCT
 - Responses remained durable in this extended follow-up, particularly for patients who achieved CR
 - Favorable OS was observed with long-term follow-up
- The adverse event profile was similar to previous reports, with no new or unexpected safety findings³
- It appears feasible to stop nivolumab after 1 year of CR and re-initiate treatment upon disease progression

References

1. Ansell SM, et al. *N Engl J Med* 2015;372:311-319; 2. Kuruvilla J, et al. *Lancet Oncol* 2018;22:512-524; 3. Armand P, et al. *J Clin Oncol* 2018;36:1428-1439; 4. Armand P, et al. *Blood* 2018;132(suppl 1):2897; 5. Younes A, et al. *Lancet Oncol* 2016;17:1283-1294.

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