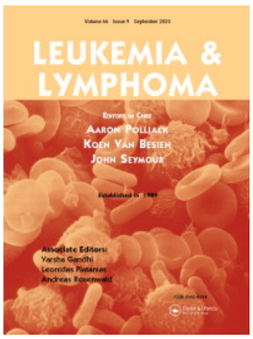

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ORIGINAL ARTICLE

Pembrolizumab in relapsed or refractory Hodgkin lymphoma: a post hoc analysis of KEYNOTE-204 by prior lines of therapy

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ABSTRACT

This report focuses on a post hoc exploratory analysis of the phase 3 KEYNOTE-204 study comparing pembrolizumab and brentuximab vedotin by number of prior lines of therapy in participants with relapsed/refractory (R/R) classical Hodgkin lymphoma (cHL). Of 304 participants randomly assigned (1:1) to pembrolizumab or brentuximab vedotin, 55 received 1 prior therapy and 249 received ≥2. For 1 prior therapy, median progression-free survival (PFS) at primary analysis (including clinical imaging data after autologous stem cell transplant [auto-SCT]) was 16.4 months with pembrolizumab and 8.4 months with brentuximab vedotin; objective response rate (ORR) was 66.7% and 53.6%. For ≥2 prior therapies, median PFS at primary analysis was 12.6 months with pembrolizumab and 8.2 months with brentuximab vedotin; ORR was 65.3% and 54.4%. Pembrolizumab improved PFS and ORR versus brentuximab vedotin regardless of prior therapies. Data suggest pembrolizumab may be a promising second-line therapy for participants with R/R cHL ineligible for auto-SCT.

Clinical trial information: ClinicalTrials.gov, NCT02684292

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Pembrolizumab; classical Hodgkin lymphoma; brentuximab vedotin

Introduction

Classical Hodgkin lymphoma (cHL) is often curable with frontline chemotherapy and/or radiation therapy; however, some patients experience relapsed or refractory (R/R) disease [1–4]. R/R cHL can pose a major therapeutic challenge, especially for patients who did not respond to autologous stem cell transplant (auto-SCT), have primary refractory disease, or are ineligible for auto-SCT [2,5–7].

Programmed cell death protein 1 (PD-1) inhibitors, including pembrolizumab and nivolumab, are approved as standard-of-care treatment options for R/R cHL [8,9]. Results from the open-label, international, randomized, phase 3 KEYNOTE-204 study (NCT02684292) showed that pembrolizumab demonstrated a statistically significant and clinically meaningful improvement in PFS when compared with brentuximab vedotin (13.2 vs 8.3 months; hazard ratio [HR], 0.65; 95% CI, 0.48–0.88; $p = 0.00271$) in participants with R/R cHL by investigator assessment who either had received auto-SCT and relapsed or were ineligible to receive auto-SCT [10]. The safety profile was consistent with that of previous reports [10].

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In the KEYNOTE-204 study, 249 of 304 participants (82%) had a median number of 3 (range, 2–11) prior therapies. Determining if the activity of pembrolizumab versus brentuximab vedotin is impacted by the number of prior therapies received before randomization is of interest to clinicians, oncologists, and hematologists. Here, we report results of a post hoc exploratory analysis of the KEYNOTE-204 study conducted to evaluate the efficacy and safety of pembrolizumab versus brentuximab vedotin in participants with R/R cHL with 1 or ≥2 prior lines of therapy.

Methods

Study design

Details of the design and key eligibility criteria of the KEYNOTE-204 study (ClinicalTrials.gov, NCT02684292) have been published [10]. In brief, eligible participants were aged ≥18 years; had R/R cHL by investigator assessment, measurable disease, and an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1; and either had received auto-SCT and relapsed or were ineligible to receive auto-SCT. Participants who responded to prior brentuximab vedotin and achieved a complete response or partial response or were naive to brentuximab vedotin were eligible. Participants who received prior therapy with an anti–PD-1 antibody were excluded. The study was conducted in accordance with principles of Good Clinical Practice and was approved by the appropriate institutional review boards and regulatory agencies. All participants provided informed consent.

Treatment

Enrolled participants were randomly assigned (1:1) to pembrolizumab 200 mg or brentuximab vedotin 1.8 mg/kg intravenously every 3 weeks. All participants were treated for ≤35 cycles or until documented disease progression, unacceptable toxicity, or investigator decision. Randomization was stratified by status after first-line therapy (primary refractory vs relapsed <12 months vs relapsed ≥12 months after end of first-line therapy) and prior auto-SCT (yes vs no).

Outcomes and assessments

Participants were evaluated by the number of prior therapies before randomization (1 and ≥2 prior therapies). The end points were progression-free survival (PFS), including clinical and imaging data after auto-SCT or allogeneic SCT (allo-SCT; primary PFS analysis); PFS, excluding clinical and imaging data after auto-SCT or allo-SCT (secondary PFS analysis); objective response rate (ORR) and duration of response (DOR) by blinded independent central review (BICR) per International Working Group criteria; and safety. Adverse events (AEs) were reported using the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0. Immune-mediated AEs, and infusion reactions were based on a prespecified list of terms and included events regardless of attribution to study treatment by the investigator.

Statistical analysis

Efficacy was evaluated in the intention-to-treat population. Safety was assessed in the all-participants-as-treated population consisting of all randomly assigned participants who received ≥1 dose of study treatment. PFS was determined using the Kaplan-Meier method for censored data. HRs were based on the stratified Cox regression model with the Efron method for handling ties, with treatment as a covariate stratified by prior auto-SCT (yes or no) and Hodgkin lymphoma status after frontline therapy (primary refractory vs relapsed <12 months after completion of frontline therapy vs relapsed ≥12 months after completion of frontline therapy). ORR was based on the Miettinen and Nurminen method stratified as previously described [10]. No adjustments were made for multiplicity. The data cutoff date was January 16, 2020.

Results

Participants and treatment

Between July 8, 2016, and July 13, 2018, 304 participants were randomly assigned to receive pembrolizumab or brentuximab vedotin. Of these, 55 participants received 1 line of therapy and 249 participants received ≥2 lines of therapy before randomization (Figure 1). Most participants received ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine)–based treatments as the first-line treatment, followed by BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, and vincristine; Supplemental Table 1). Among the 55 participants with 1 prior line of therapy, 27 were randomly assigned to receive pembrolizumab and 28 to receive brentuximab vedotin. Among the 249 participants with ≥2 prior lines of therapy, 124 were randomly assigned to receive pembrolizumab and 125 to receive brentuximab vedotin. The baseline characteristics between the 2 subgroups were generally well balanced between treatment arms (Table 1). For participants who received 1 prior line of therapy,

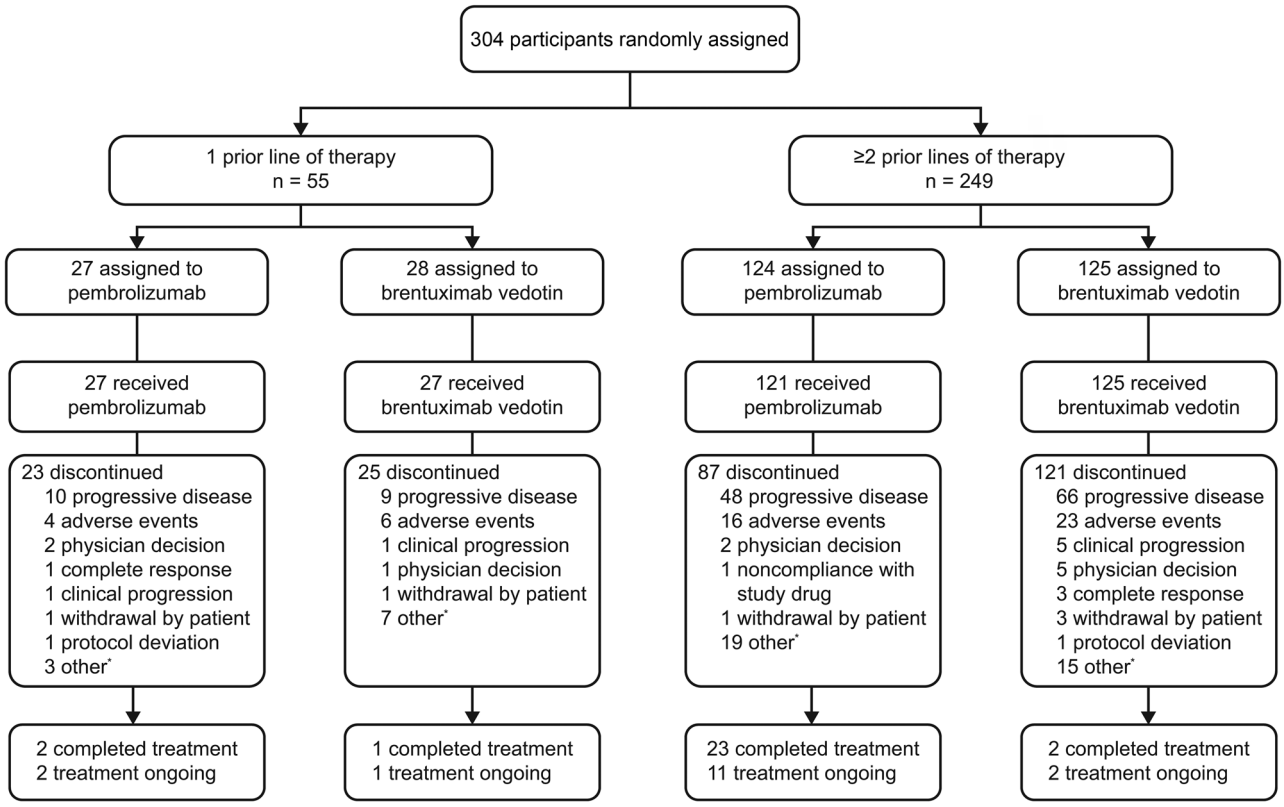

Figure 1. Trial profile.
*Other reasons include bone marrow transplant, excluded medication, and nonstudy anticancer therapy.

no participant received treatment with brentuximab vedotin and all participants were considered ineligible for auto-SCT due to chemorefractory disease, comorbidities, and age in the majority of participants. For participants with ≥2 prior lines of therapy, 56 participants (45.2%) had received prior auto-SCT in the pembrolizumab arm and 56 participants (44.8%) received prior auto-SCT in the brentuximab vedotin arm.

For participants who received 1 prior line of therapy, all participants in the pembrolizumab arm and 27 of 28 participants (96.4%) in the brentuximab vedotin arm received ≥1 dose of study treatment (Figure 1). The median time from randomization to data cutoff for all participants was 23.9 months (range, 18.2–34.8). The median duration of treatment was 294.0 days (range, 64.0–725.0) with pembrolizumab and 128.0 days (range, 1.0–721.0) with brentuximab vedotin; the median number of treatment cycles was 15.0 (range, 4.0–35.0) and 7.0 (range, 1.0–35.0), respectively. A total of 23 participants (85.2%) receiving pembrolizumab and 25 participants (92.6%) receiving brentuximab vedotin discontinued treatment, most commonly owing to progressive disease (10 participants [37.0%] and 9 participants [33.3%], respectively) (Figure 1).

For participants who received ≥2 prior lines of therapy, 121 of 124 participants (97.6%) in the pembrolizumab arm and 125 participants (100%) in the brentuximab vedotin arm received ≥1 dose of study treatment (Figure 1). The median time from randomization to data cutoff for the total population was 27.4 months (range, 18.2–42.3). The median duration of treatment was 324.0 days (range, 1.0–814.0) with pembrolizumab and 148.0 days (range, 1.0–794.0) with brentuximab vedotin; the median number of treatment cycles was 16.0 (range, 1.0–35.0) and 7.0 (range, 1.0–35.0), respectively. A total of 87 participants (71.9%) receiving pembrolizumab and 121 participants (96.8%) receiving brentuximab vedotin discontinued treatment, most commonly due to progressive disease (48 participants [39.7%] and 66 participants [52.8%], respectively) (Figure 1).

Efficacy

For participants who received 1 prior line of therapy, the median PFS by BICR at the primary PFS analysis was 16.4 months (95% CI, 8.3-not reached [NR]) with pembrolizumab and 8.4 months (95% CI, 5.4-NR) with brentuximab vedotin (Figure 2A). The median PFS at the secondary PFS analysis was 11.7 months (95% CI, 8.2-NR) with pembrolizumab and 8.3 months (95% CI, 5.4–16.8) with brentuximab vedotin (Figure 3A). The

Table 1. Baseline characteristics.

	1 prior line of therapy		≥2 prior lines of therapy	
	Pembrolizumab (*n* = 27)	Brentuximab vedotin (*n* = 28)	Pembrolizumab (*n* = 124)	Brentuximab vedotin (*n* = 125)
Median age (range), years	47.0 (22–84)	50.0 (22–81)	34.5 (18–79)	34.0 (18–83)
<65	15 (55.6)	18 (64.3)	109 (87.9)	113 (90.4)
≥65	12 (44.4)	10 (35.7)	15 (12.1)	12 (9.6)
Sex				
Male	17 (63.0)	17 (60.7)	67 (54.0)	73 (58.4)
Female	10 (37.0)	11 (39.3)	57 (46.0)	52 (41.6)
Geographical region				
North America	4 (14.8)	5 (17.9)	23 (18.5)	25 (20.0)
Europe	9 (33.3)	11 (39.3)	40 (32.3)	35 (28.0)
Japan	3 (11.1)	2 (7.1)	6 (4.8)	5 (4.0)
Other	11 (40.7)	10 (35.7)	55 (44.4)	60 (48.0)
ECOG PS				
0	18 (66.7)	23 (82.1)	68 (54.8)	77 (61.6)
1	9 (33.3)	5 (17.9)	55 (44.4)	48 (38.4)
2	0 (0)	0 (0)	1 (0.8)	0 (0)
Previous auto-SCT				
Yes	0 (0)	0 (0)	56 (45.2)	56 (44.8)
No	27 (100)	28 (100)	68 (54.8)	69 (55.2)
Disease status after frontline therapy				
Primary refractory	11 (40.7)	7 (25.0)	50 (40.3)	55 (44.0)
Relapsed <12 months	10 (37.0)	8 (28.6)	32 (25.8)	34 (27.2)
Relapsed ≥12 months	6 (22.2)	13 (46.4)	42 (33.9)	36 (28.8)
Previous brentuximab vedotin	0 (0)	0 (0)	5 (4.0)[a]	10 (8.0)[b]
Previous radiotherapy	3 (11.1)	5 (17.9)	55 (44.4)	56 (44.8)
Bulky disease	6 (22.2)	2 (7.1)	29 (23.4)	23 (18.4)
Baseline B symptoms[c]	5 (18.5)	4 (14.3)	38 (30.6)	32 (25.6)
Baseline bone marrow involvement	4 (14.8)	2 (7.1)	8 (6.5)	3 (2.4)

Data are *n* (%) unless otherwise specified.
Auto-SCT, autologous stem cell transplantation; ECOG PS, Eastern Cooperative Oncology Group performance status.
[a]Four participants had a best response of complete response, and 1 had a partial response to prior treatment with brentuximab vedotin by investigator review.
[b]Seven participants had a best response of complete response, and 3 had a partial response to prior treatment with brentuximab vedotin by investigator review.
[c]B symptoms include unintentional weight loss; unexplained, persistent, or recurrent fever with temperatures above 38 °C; and recurrent night sweats.

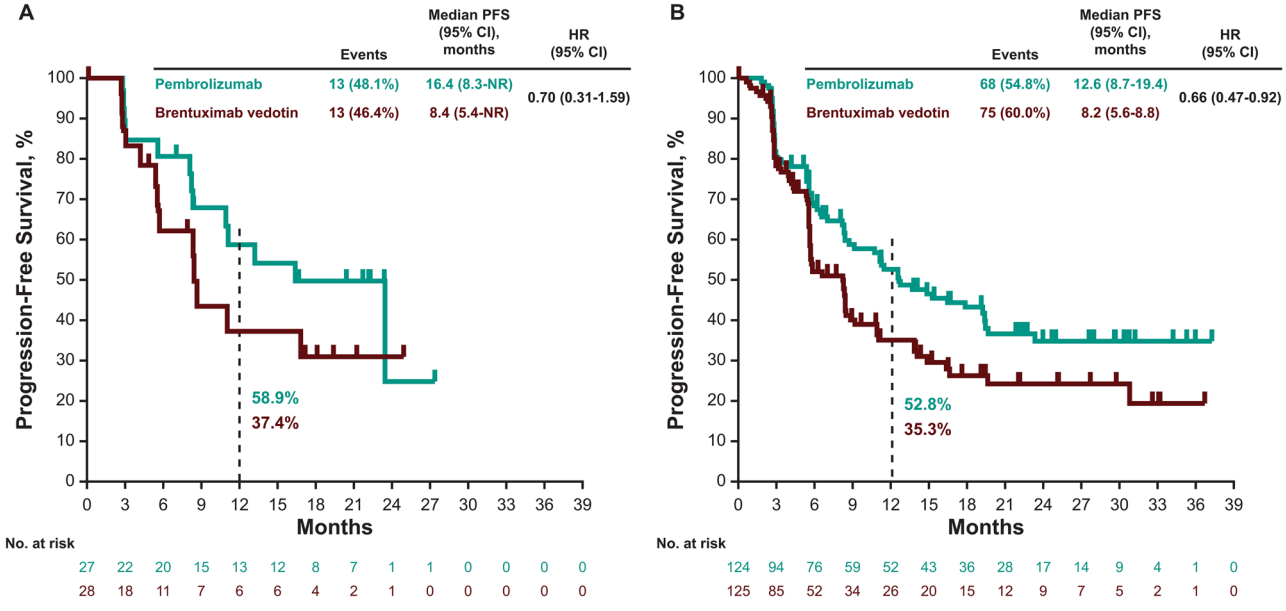

Figure 2. Primary progression-free survival (PFS) analysis by blinded independent central review per International Working Group 2007 criteria. PFS including clinical imaging data following auto-SCT or allo-SCT for (A) participants with 1 prior line of therapy or (B) participants with ≥2 prior lines of therapy. Primary PFS analysis was defined as PFS including clinical and imaging data after auto-SCT or allo-SCT. allo-SCT, allogeneic stem cell transplantation; auto-SCT, autologous stem cell transplantation; HR, hazard ratio; NR, not reached.

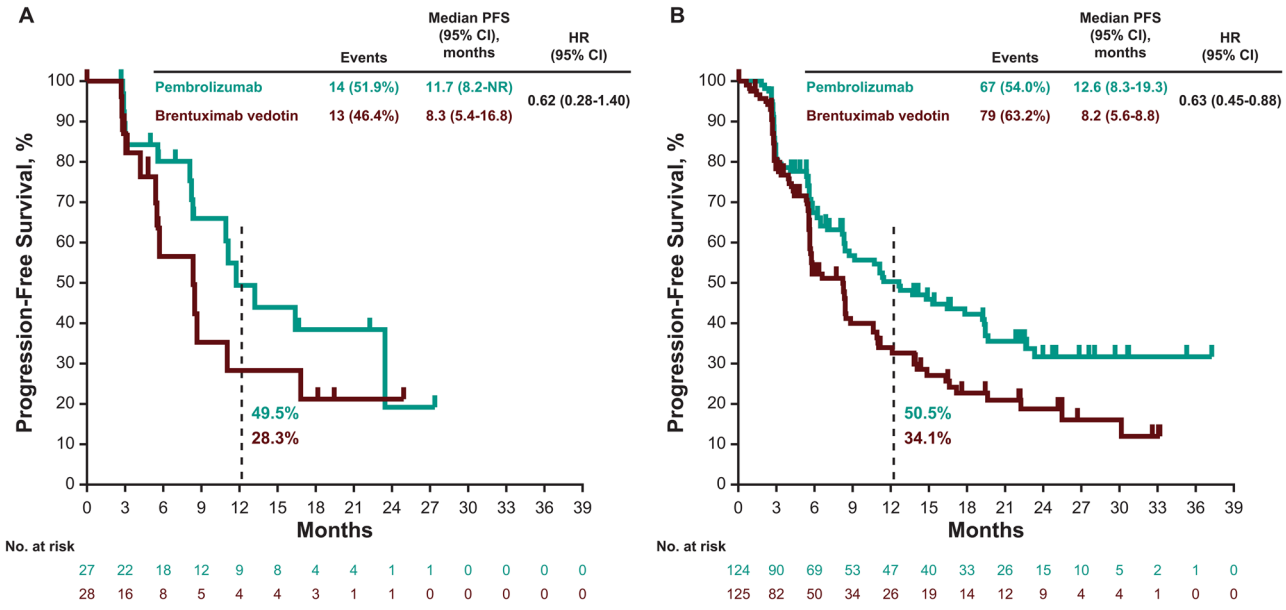

Figure 3. Secondary progression-free survival (PFS) analysis by blinded independent central review per International Working Group 2007 criteria. PFS excluding clinical imaging data following auto-SCT or allo-SCT (secondary PFS analysis) for (A) participants with 1 prior line of therapy or (B) participants with ≥2 prior lines of therapy. Secondary PFS analysis was defined as PFS excluding clinical and imaging data after auto-SCT or allo-SCT. allo-SCT, allogeneic stem cell transplantation; auto-SCT, autologous stem cell transplantation; HR, hazard ratio; NR, not reached.

Table 2. Objective response as assessed by blinded independent central review by International Working Group 2007 criteria.

	1 prior line of therapy		≥2 prior lines of therapy	
	Pembrolizumab ($n=27$)	Brentuximab vedotin ($n=28$)	Pembrolizumab ($n=124$)	Brentuximab vedotin ($n=125$)
ORR, % (95% CI)	66.7 (46.0–83.5)	53.6 (33.9–72.5)	65.3 (56.3–73.6)	54.4 (45.3–63.3)
Difference, estimate (95% CI)	13.7 (–13.6 to 38.8)		10.5 (–1.8 to 22.5)	
Best overall response, *n* (%)				
CR	4 (14.8)	10 (35.7)	33 (26.6)	27 (21.6)
PR	14 (51.9)	5 (17.9)	48 (38.7)	41 (32.8)
SD	6 (22.2)	7 (25.0)	15 (12.1)	29 (23.2)
PD	3 (11.1)	4 (14.3)	23 (18.5)	24 (19.2)
Not evaluable	0 (0)	0 (0)	1 (0.8)	1 (0.8)
No assessment	0 (0)	2 (7.1)	4 (3.2)	3 (2.4)

CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

ORR was 66.7% (95% CI, 46.0–83.5) with pembrolizumab and 53.6% (95% CI, 33.9–72.5) with brentuximab vedotin (Table 2). Complete responses occurred in 4 participants (14.8%) in the pembrolizumab arm and in 10 participants (35.7%) in the brentuximab vedotin arm; partial responses occurred in 14 participants (51.9%) and 5 participants (17.9%), respectively. The median DOR was 20.7 months (range, 2.8 to 20.7) with pembrolizumab and 14.1 months (range, 0.0+ to 21.9+) with brentuximab vedotin (Supplemental Figure 1A). An estimated 64.9% of participants who responded to pembrolizumab and 52.2% of participants who responded to brentuximab vedotin had a response duration of ≥12 months. Auto-SCT was a component of subsequent treatment for 7 participants (25.9%) in the pembrolizumab arm and 9 participants (33.3%) in the brentuximab vedotin arm; 1 participant (3.7%) in the brentuximab vedotin arm received subsequent allo-SCT.

For participants who received ≥2 prior lines of therapy, the median PFS by BICR at the primary PFS analysis was 12.6 months (95% CI, 8.7–19.4) with pembrolizumab and 8.2 months (95% CI, 5.6–8.8) with brentuximab vedotin (Figure 2B). The median PFS at the secondary PFS analysis was 12.6 months (95% CI, 8.3–19.3) with pembrolizumab and 8.2 months (95% CI, 5.6–8.8) with brentuximab vedotin (Figure 3B). The ORR was 65.3% (95% CI, 56.3–73.6) with pembrolizumab and 54.4% (95% CI, 45.3–63.3) with brentuximab vedotin (Table 2). Complete responses occurred in 33 participants (26.6%) in the pembrolizumab arm and 27 participants (21.6%) in the brentuximab vedotin arm; partial responses occurred in 48 participants

(38.7%) and 41 participants (32.8%), respectively. The median DOR was 20.5 months (range, 0.0+ to 33.2+) with pembrolizumab and 11.2 months (range, 0.0+ to 33.9+) with brentuximab vedotin (Supplemental Figure 1B). An estimated 61.7% of participants who had a response to pembrolizumab and 49.0% with a response to brentuximab vedotin had a response duration of ≥12 months. Auto-SCT was a component of subsequent treatment for 23 participants (19.0%) in the pembrolizumab arm and 25 participants (20.0%) in the brentuximab vedotin arm; 14 participants (11.6%) and 12 participants (9.6%) received subsequent allo-SCT, respectively.

Safety

For participants who received 1 prior line of therapy and ≥1 dose of study treatment, 21 participants (77.8%) in the pembrolizumab arm and 20 participants (74.1%) in the brentuximab vedotin arm (Table 3) experienced a treatment-related AE. The most common treatment-related AEs for participants in the pembrolizumab arm (incidence ≥10%) were hyperthyroidism (22.2%), hypothyroidism (18.5%), pyrexia (18.5%), pruritus (14.8%), and decreased appetite (11.1%); the most common treatment-related AEs for those in the brentuximab vedotin arm were peripheral neuropathy (22.2%), nausea (18.5%), fatigue (14.8%), pruritus (14.8%), and peripheral sensory neuropathy (11.1%). Grade 3 treatment-related AEs occurred in 1 participant (3.7%) in the pembrolizumab arm and 8 participants (29.6%) in the brentuximab vedotin arm. Treatment-related AEs leading to discontinuation were reported in 4 participants (14.8%) and 6 participants (22.2%), respectively. No treatment-related deaths were reported in either arm. Immune-mediated AEs and infusion reactions were reported in 9 participants (33.3%) in the pembrolizumab arm and 2 participants (7.4%) in the brentuximab vedotin arm (Supplemental Table 2). No participant discontinued treatment due to an immune-mediated AE or infusion reaction.

For participants who received ≥2 prior lines of therapy and ≥1 dose of study treatment, treatment-related AEs were reported in 89 participants (73.6%) with pembrolizumab and 97 participants (77.6%) with brentuximab vedotin (Table 4). The most common treatment-related AEs for participants in the pembrolizumab arm (incidence ≥10%) were hypothyroidism (14.9%), diarrhea (11.6%), and pyrexia (11.6%); the most common for those in the brentuximab vedotin arm were peripheral neuropathy (17.6%), peripheral sensory neuropathy (13.6%), nausea (12.0%), vomiting (11.2%), and neutropenia (10.4%). Grade 3–5

Table 3. Treatment-related adverse events (incidence ≥5% in either arm and corresponding grade 3 events) for participants with 1 prior line of therapy.

	Pembrolizumab ($n=27$)		Brentuximab vedotin ($n=27$)	
	Any grade	Grade 3[a]	Any grade	Grade 3[a]
Any adverse event	21 (77.8)	1 (3.7)	20 (74.1)	8 (29.6)
Hyperthyroidism	6 (22.2)	0 (0)	0 (0)	0 (0)
Hypothyroidism	5 (18.5)	0 (0)	1 (3.7)	0 (0)
Pyrexia	5 (18.5)	1 (3.7)	0 (0)	0 (0)
Pruritus	4 (14.8)	0 (0)	4 (14.8)	0 (0)
Decreased appetite	3 (11.1)	0 (0)	2 (7.4)	0 (0)
Chills	2 (7.4)	0 (0)	0 (0)	0 (0)
Constipation	2 (7.4)	0 (0)	1 (3.7)	0 (0)
Oropharyngeal pain	2 (7.4)	0 (0)	0 (0)	0 (0)
Pneumonitis	2 (7.4)	0 (0)	0 (0)	0 (0)
Peripheral neuropathy	0 (0)	0 (0)	6 (22.2)	4 (14.8)
Fatigue	1 (3.7)	0 (0)	4 (14.8)	0 (0)
Peripheral sensory neuropathy	1 (3.7)	0 (0)	3 (11.1)	1 (3.7)
Arthralgia	1 (3.7)	0 (0)	2 (7.4)	0 (0)
Nausea	0 (0)	0 (0)	5 (18.5)	0 (0)
Bone pain	0 (0)	0 (0)	2 (7.4)	0 (0)
Neutropenia	0 (0)	0 (0)	2 (7.4)	1 (3.7)
Neutrophil count decreased	0 (0)	0 (0)	2 (7.4)	2 (7.4)
Gamma-glutamyltransferase level increased	0 (0)	0 (0)	2 (7.4)	1 (3.7)
Paresthesia	0 (0)	0 (0)	2 (7.4)	0 (0)

Data are *n* (%).
[a]No grade 4 or 5 adverse events occurred.

Table 4. Treatment-related adverse events (incidence ≥5% in either arm and corresponding grade 3–5 events) for participants with ≥2 prior lines of therapy.

	Pembrolizumab ($n=121$)		Brentuximab vedotin ($n=125$)	
	Any grade	Grade 3–5[a]	Any grade	Grade 3–5[b]
Any adverse event	89 (73.6)	28 (23.1)	97 (77.6)	30 (24.0)
Hypothyroidism	18 (14.9)	0 (0)	1 (0.8)	0 (0)
Diarrhea	14 (11.6)	2 (1.7)	5 (4.0)	0 (0)
Pyrexia	14 (11.6)	0 (0)	9 (7.2)	0 (0)
Fatigue	12 (9.9)	0 (0)	12 (9.6)	0 (0)
Pruritus	12 (9.9)	0 (0)	4 (3.2)	0 (0)
Pneumonitis	10 (8.3)	6 (5.0)	1 (0.8)	1 (0.8)
Rash	8 (6.6)	0 (0)	7 (5.6)	0 (0)
Arthralgia	6 (5.0)	0 (0)	5 (4.0)	0 (0)
Nausea	6 (5.0)	0 (0)	15 (12.0)	0 (0)
Thrombocytopenia	6 (5.0)	2 (1.7)	5 (4.0)	0 (0)
Vomiting	6 (5.0)	1 (0.8)	14 (11.2)	0 (0)
Peripheral neuropathy	3 (2.5)	1 (0.8)	22 (17.6)	1 (0.8)
Peripheral sensory neuropathy	2 (1.7)	0 (0)	17 (13.6)	1 (0.8)
Neutropenia	5 (4.1)	3 (2.5)	13 (10.4)	10 (8.0)
Infusion reaction	5 (4.1)	0 (0)	12 (9.6)	3 (2.4)
Neutrophil count decreased	3 (2.5)	1 (0.8)	8 (6.4)	5 (4.0)
Paresthesia	2 (1.7)	0 (0)	8 (6.4)	2 (1.6)
Anemia	1 (0.8)	1 (0.8)	7 (5.6)	1 (0.8)
Constipation	1 (0.8)	0 (0)	7 (5.6)	0 (0)

Data are *n* (%).
[a]One grade 5 adverse event occurred (pneumonia). Grade 4 events occurred in 5 participants with some participants experiencing more than 1 adverse event (3 pneumonitis, 2 acute kidney injury, 2 immune thrombocytopenic purpura, 1 myocarditis, 1 encephalitis autoimmune, 1 hepatic function abnormal, 1 nephritis).
[b]No grade 5 adverse events occurred. Grade 4 events occurred in 6 participants (3 neutropenia, 1 neutrophil count decreased, 1 hypovolemic shock, 1 tubulointerstitial nephritis).

treatment-related AEs occurred in 28 participants (23.1%) in the pembrolizumab arm and 30 participants (24.0%) in the brentuximab vedotin arm. Treatment-related AEs leading to discontinuation were reported in 15 participants (12.4%) and 19 participants (15.2%), respectively. No treatment-related deaths were reported in the brentuximab vedotin arm; however, 1 participant died from pneumonia in the pembrolizumab arm. Immune-mediated AEs and infusion reactions were reported in 44 participants (36.4%) in the pembrolizumab arm and 19 participants (15.2%) in the brentuximab vedotin arm (Supplemental Table 3). Immune-mediated AEs and infusion reactions leading to discontinuation were reported in 1 participant (0.8%) and 3 participants (2.4%), respectively.

Discussion

In this post hoc analysis of the KEYNOTE-204 study, pembrolizumab monotherapy resulted in a numerically longer PFS and higher ORR than brentuximab vedotin in participants with R/R cHL regardless of the number of prior therapies, which is consistent with the results observed at the primary analysis [10]. The ORR in the pembrolizumab arm was similar regardless of the number of prior therapies. In the primary PFS analysis, pembrolizumab appeared to provide a longer PFS for participants with 1 prior line of therapy (16.4 months vs 12.6 months); however, this difference needs to be interpreted with caution given that most participants (249/304; 81.9%) in KEYNOTE-204 received ≥2 prior lines of therapy. Notably, in a real-world, retrospective study, patients who received checkpoint inhibitors as the first treatment after auto-SCT had a significantly higher post-progression survival compared with those who did not receive checkpoint inhibitors as first treatment and tended to have a higher post-progression survival compared with those who received brentuximab vedotin [11].

Analyses from other studies of PD-1 inhibitors such as KEYNOTE-087 and CheckMate 205 focused on heavily pretreated participants with R/R cHL after auto-SCT and treatment with brentuximab vedotin. Data for participants with ≥2 prior lines of therapy from KEYNOTE-204 were comparable; however, the majority of participants (~86%) from KEYNOTE-087 and CheckMate 205 had ≥3 prior lines of therapy [12,13]. Overall, the KEYNOTE-087 study showed antitumor activity and durable responses with an ORR of 71.4% and a median PFS of 13.7 months for pembrolizumab. The ORR for cohort 1 of this study was 78.3% in participants whose disease did not respond to or progressed after auto-SCT and subsequent brentuximab vedotin, and the ORR for cohort 3 was 73.3% in participants who did not respond to or whose disease progressed after auto-SCT and did not receive brentuximab vedotin; the median PFS was 16.4 months and 19.7 months, respectively. Similarly, the CheckMate 205 study showed durable responses with nivolumab and reported an overall ORR of 69% and a median PFS of 14.7 months. The ORR for cohort B of this study was 68% in participants who did not respond to brentuximab vedotin treatment after auto-SCT, and the ORR for cohort C was 73% in participants who were treated with brentuximab vedotin before and/or after auto-SCT treatment failure; the median PFS was 14.7 months and 11.9 months, respectively. Data for participants with 1 prior line of therapy from KEYNOTE-204 were comparable with participant data from cohort 2 of KEYNOTE-087, which enrolled participants who were unresponsive to salvage chemotherapy, did not receive auto-SCT, and were treated with pembrolizumab; results were also comparable with data from cohort A of CheckMate 205, which enrolled participants who were naive to brentuximab vedotin and then were treated with nivolumab [12,13]. The ORRs for cohort 2 of KEYNOTE-087 and cohort A of CheckMate 205 were 64.2% and 65%, and the median PFS was 11.1 months and 18.3 months, respectively. However, data should be interpreted with caution as both of these study cohorts enrolled participants who were heavily pretreated, and participants in cohort 2 of KEYNOTE-087 received prior treatment with brentuximab vedotin [12,13].

Auto-SCT is the standard-of-care treatment for eligible patients with relapsed cHL [14]. Notably, achieving a complete response prior to transplant has resulted in superior outcomes in this population [14]. Several studies have indicated a potential role for pembrolizumab and brentuximab vedotin in this setting either when combined or when administered with chemotherapy or other PD-1 inhibitors such as nivolumab [15–23]. Data remain limited in the second-line treatment setting for patients with R/R cHL and are not intended for auto-SCT–based approaches either due to refractory disease or age and comorbidity. Based on smaller retrospective studies, brentuximab vedotin became a standard-of-care treatment for patients ineligible for second-line auto-SCT because these patients were not included in the phase 2 study of brentuximab vedotin in R/R cHL [24–26]. KEYNOTE-204 is the only prospective randomized study that includes participants ineligible for second-line treatment with auto-SCT and establishes pembrolizumab as a standard for this underserved patient population.

The safety profiles of pembrolizumab and brentuximab vedotin were generally similar to those reported for each agent, regardless of number of prior therapies, and no unexpected safety signals were observed [12,27,28].

Fewer grade 3–5 events occurred in participants with 1 prior line of therapy than in those with ≥2 prior lines of therapy in the pembrolizumab arm; 1 participant (3.7%) experienced a grade 3 event versus 28 participants (23.1%) who experienced grade 3–5 events.

Limitations of this study include that it is a post hoc analysis of a randomized trial and the small sample size for participants with 1 prior line of therapy compared with participants with ≥2 prior lines of therapy. Furthermore, the current study was not powered for definitive demonstration of efficacy in any subgroups, and the number of prior lines of therapy was not a stratification factor. Notably, comparison of response rate and PFS by lines of therapy were not the objectives of this post hoc analysis, and the sample size for participants with 1 prior line of therapy was considered relatively small compared with that of participants with ≥2 prior lines of therapy. Therefore, the results should be interpreted with caution. Conducting randomized controlled trials for all of these distinct subpopulations remains a challenge; however, KEYNOTE-204 compared pembrolizumab with brentuximab vedotin, which was the standard of care for all these populations. It is also important to recognize that both brentuximab vedotin and PD-1 inhibitors are increasingly being used earlier in the treatment of cHL, particularly in the curative setting, and that treatment standards for R/R disease will need to evolve. Additionally, there is also the potential of combinations of pembrolizumab with chemotherapy, brentuximab vedotin, or lymphocyte-activation gene 3 antibodies, which are currently being evaluated for R/R disease [21,29–31]. Notably, the S1826 study of nivolumab plus doxorubicin, vinblastine, and dacarbazine (AVD) has changed the treatment paradigm for patients with advanced-stage cHL by demonstrating superior efficacy, improved tolerability, and low rate of radiation usage compared with brentuximab vedotin. Based on these results, nivolumab plus AVD is a new standard of care and has established the key role of PD-1 blockade in the initial treatment of cHL [32,33].

In conclusion, findings from the KEYNOTE-204 confirm that patients with R/R cHL benefit from pembrolizumab monotherapy regardless of prior line of therapy. As a result, pembrolizumab monotherapy is an important option as a second-line therapy for patients with R/R cHL who are ineligible for auto-SCT.

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Author contributions

P.M. conceived, designed, or planned the study; E.P.-K., R.G., N.A.J., I.G., V.B., G.F.P., N.G., and I.K. acquired the data; J.K., D.M., A.S., J. de O., G.F.P., I.K., J.L., R.Y., P.M., P.L.Z. analyzed the data; J.K., D.M., A.S., E.P.-K., R.G., L.M.F., N.S., J.L., R.Y., P.M., and P.L.Z. interpreted the results; J.K. drafted the manuscript; J.K., D.M, A.S.; E.P.-K., R.G., N.A.J., L.M.F., J. de O., V.B., G.F.P., N.G., I.K., N.S., J.L., R.Y., P.M., and P.L.Z. critically reviewed or revised the manuscript for important intellectual content; all authors had final approval of the manuscript version to be published.

Disclosure statement

J.K. declares honoraria with AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Genmab Gilead, GSK, Incyte, Janssen, Karyopharm, MSD, Novartis, Pfizer, Roche, and Seattle Genetics; advisory/consultancy roles with AbbVie, Bristol Myers Squibb, Gilead/Kite, MSD, Roche, and Seattle Genetics; research funding from AstraZeneca, MSD, Novartis, and Roche; and other from Karyopharm (DSMB). D.M. declares advisory/consultancy roles with ADC Therapeutics, Daiichi Sankyo (spouse), Genmab, and Seagen; speakers bureau roles for BeiGene; expert testimony for AstraZeneca; research funding from Genentech, Genmab, Karyopharm, and AstraZeneca (spouse); and full/part-time employment with Karmanos Cancer Institute, Detroit, MI. A.S. declares advisory roles for Bayer, Bristol Myers Squibb, Eisai, Gilead, MSD, Pfizer, and Servier; consultancy roles for Incyte and Sanofi; and speakers bureau for AbbVie, Amgen, AstraZenenca, Bayer, Bristol Myers Squibb, Celgene, Eisai, Gilead, Lilly, MSD, Novartis, Pfizer, Roche, Sandoz, Servier, and Takeda.; and travel/accommodation/expenses from BeiGene, Roche, and Takeda. R.G. declares honoraria with AbbVie, Astellas, Gilead, Janssen, MSD, Novartis, Otsuka, Pfizer, and Takeda. N.A.J. declares honoraria with AbbVie, Incyte, MSD, and Roche; advisory/consultancy roles with AbbVie, AstraZeneca, BeiGene, Bristol Myers Squibb, Gilead, Incyte, Janssen, MSD, Roche, and Seagen; and research funding from Gilead, Incyte, and Roche. V.B. declares advisory/consultancy role with MSD; speaker bureau for Janssen; and research funding from AstraZeneca, MSD, and Takeda. G.F.P. declares honoraria, advisory/consultancy roles, speakers bureau, and travel/accommodation/expenses with/from AstraZeneca, BeiGene, Knight Therapeutics, Lilly, MSD, Roche, and Takeda. I.K. declares advisory/consultancy roles, speakers bureau roles, expert testimony, and leadership roles with AbbVie, AstraZeneca, Biopharma, Janssen, Roche, and Takeda; research funding from AbbVie, Acerta Pharma, Bayer, Cromos Pharma, GlaxoSmithKline, InnoCare Pharma, MSD, MorphoSys AG, Pharmacyclics, and Takeda; and travel/accommodation/expenses from AstraZeneca; full/part-time employment with National Cancer Institute, Kyiv, Ukraine. N.S. declares honoraria with BeiGene, Janssen and Ono; and research funding from Incyte Biosciences Japan, Janssen, Mitsubishi Tanabe Pharma Corporation, MSD, and Ono. J.L. declares employment from Merck Sharp & Dohme LLC, a subsidiary of Merck

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Data-sharing statement

Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD), is committed to providing qualified scientific researchers access to anonymized data and clinical study reports from the company's clinical trials for the purpose of conducting legitimate scientific research. MSD is also obligated to protect the rights and privacy of trial participants and, as such, has a procedure in place for evaluating and fulfilling requests for sharing company clinical trial data with qualified external scientific researchers. The MSD data-sharing website (available at: https://externaldatasharing-msd.com/) outlines the process and requirements for submitting a data request. Applications will be promptly assessed for completeness and policy compliance. Feasible requests will be reviewed by a committee of MSD subject matter experts to assess the scientific validity of the request and the qualifications of the requestors. In line with data privacy legislation, submitters of approved requests must enter into a standard data-sharing agreement with MSD before data access is granted. Data will be made available for request after product approval in the USA and EU or after product development is discontinued. There are circumstances that may prevent MSD from sharing requested data, including country or region-specific regulations. If the request is declined, it will be communicated to the investigator. Access to genetic or exploratory biomarker data requires a detailed, hypothesis-driven statistical analysis plan that is collaboratively developed by the requestor and MSD subject matter experts; after approval of the statistical analysis plan and execution of a data-sharing agreement, MSD will either perform the proposed analyses and share the results with the requestor or will construct biomarker covariates and add them to a file with clinical data that is uploaded to an analysis portal so that the requestor can perform the proposed analyses.

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References

[1] Borchmann S, von Tresckow B. Novel agents in classical Hodgkin lymphoma. Leuk Lymphoma. 2017;58(10):2275–2286. doi:10.1080/10428194.2017.1300898

[2] Cheah CY, Chihara D, Horowitz S, et al. Patients with classical Hodgkin lymphoma experiencing disease progression after treatment with brentuximab vedotin have poor outcomes. Ann Oncol. 2016;27(7):1317–1323. doi:10.1093/annonc/mdw169

[3] Lo AC, Dieckmann K, Pelz T, et al. Pediatric classical Hodgkin lymphoma. Pediatr Blood Cancer. 2021;68 Suppl 2(S2):e28562. doi:10.1002/pbc.28562

[4] Meti N, Esfahani K, Johnson NA. The role of immune checkpoint inhibitors in classical Hodgkin lymphoma. Cancers (Basel). 2018;10(6):204. doi:10.3390/cancers10060204

[5] Santoro A, Mazza R, Pulsoni A, et al. Five-year results of the BEGEV salvage regimen in relapsed/refractory classical Hodgkin lymphoma. Blood Adv. 2020;4(1):136–140. doi:10.1182/bloodadvances.2019000984

[6] Fermé C, Mounier N, Diviné M, et al. Intensive salvage therapy with high-dose chemotherapy for patients with advanced Hodgkin's disease in relapse or failure after initial chemotherapy: results of the Groupe d'Etudes des Lymphomes de l'Adulte H89 Trial. J Clin Oncol. 2002;20(2):467–475. doi:10.1200/jco.2002.20.2.467

[7] Goodman KA, Riedel E, Serrano V, et al. Long-term effects of high-dose chemotherapy and radiation for relapsed and refractory Hodgkin's lymphoma. J Clin Oncol. 2008;26(32):5240–5247. doi:10.1200/jco.2007.15.5507

[8] KEYTRUDA® (pembrolizumab) injection, for intravenous use. 01/2025. Rahway, NJ, USA: Merck Sharp & Dohme LLC; 2025.

[9] OPDIVO (nivolumab) injection, for intravenous use. 05/2022. Princeton (NJ): Bristol Myers Squibb Company; 2022.

[10] Kuruvilla J, Ramchandren R, Santoro A, et al. Pembrolizumab versus brentuximab vedotin in relapsed or refractory classical Hodgkin lymphoma (KEYNOTE-204): an interim analysis of a multicentre, randomised, open-label, phase 3 study. Lancet Oncol. 2021;22(4):512–524. doi:10.1016/s1470-2045(21)00005-x

[11] Desai SH, Spinner MA, Evens AM, et al. Overall survival of patients with cHL who progress after autologous stem cell transplant: results in the novel agent era. Blood Adv. 2023;7(23):7295–7303. doi:10.1182/bloodadvances.2023011205

[12] Armand P, Zinzani PL, Lee HJ, et al. Five-year follow-up of KEYNOTE-087: pembrolizumab monotherapy in relapsed/refractory classical Hodgkin lymphoma. Blood. 2023;142(10):878–886. doi:10.1182/blood.2022019386

[13] Armand P, Engert A, Younes A, et al. Nivolumab for relapsed/refractory classic hodgkin lymphoma after failure of autologous hematopoietic cell transplantation: extended follow-up of the multicohort single-arm phase II CheckMate 205 trial. J Clin Oncol. 2018;36(14):1428–1439. doi:10.1200/jco.2017.76.0793

[14] Sureda A, André M, Borchmann P, et al. Improving outcomes after autologous transplantation in relapsed/refractory Hodgkin lymphoma: a European expert perspective. BMC Cancer. 2020;20(1):1088. doi:10.1186/s12885-020-07561-2

[15] Herrera AF, Moskowitz AJ, Bartlett NL, et al. Interim results of brentuximab vedotin in combination with nivolumab in patients with relapsed or refractory Hodgkin lymphoma. Blood. 2018;131(11):1183–1194. doi:10.1182/blood-2017-10-811224

[16] Advani RH, Moskowitz AJ, Bartlett NL, et al. Brentuximab vedotin in combination with nivolumab in relapsed or refractory Hodgkin lymphoma: 3-year study results. Blood. 2021;138(6):427–438. doi:10.1182/blood.2020009178

[17] Lynch RC, Cassaday RD, Smith SD, et al. Dose-dense brentuximab vedotin plus ifosfamide, carboplatin, and etoposide for second-line treatment of relapsed or refractory classical Hodgkin lymphoma: a single centre, phase 1/2 study. Lancet Haematol. 2021;8(8):e562–e71. doi:10.1016/s2352-3026(21)00170-8

[18] Moskowitz AJ, Shah G, Schöder H, et al. Phase II trial of pembrolizumab plus gemcitabine, vinorelbine, and liposomal doxorubicin as second-line therapy for relapsed or refractory classical Hodgkin lymphoma. J Clin Oncol. 2021;39(28):3109–3117. doi:10.1200/jco.21.01056

[19] Massaro F, Meuleman N, Bron D, et al. Brentuximab vedotin and pembrolizumab combination in patients with relapsed/refractory hodgkin lymphoma: a single-centre retrospective analysis. Cancers (Basel). 2022;14(4):982. doi:10.3390/cancers14040982

[20] Mei MG, Lee HJ, Palmer JM, et al. Response-adapted anti-PD-1-based salvage therapy for Hodgkin lymphoma with nivolumab alone or in combination with ICE. Blood. 2022;139(25):3605–3616. doi:10.1182/blood.2022015423

[21] Bryan LJ, Casulo C, Allen PB, et al. Pembrolizumab added to ifosfamide, carboplatin, and etoposide chemotherapy for relapsed or refractory classic Hodgkin lymphoma: a multi-institutional phase 2 investigator-initiated nonrandomized clinical trial. JAMA Oncol. 2023;9(5):683–691. doi:10.1001/jamaoncol.2022.7975

[22] Desai SH, Spinner MA, David K, et al. Checkpoint inhibitor-based salvage regimens prior to autologous stem cell transplant improve event-free survival in relapsed/refractory classic Hodgkin lymphoma. Am J Hematol. 2023;98(3):464–471. doi:10.1002/ajh.26827

[23] Diefenbach CS, Jegede O, Ansell SM, et al. Results from an intergroup randomized phase II study of the combinations of ipilimumab, nivolumab and brentuximab vedotin in patients with relapsed/refractory classic Hodgkin lymphoma: a trial of the ECOG-ACRIN research group (E4412). Blood. 2023;142(Supplement 1):607. doi:10.1182/blood-2023-184531

[24] Zinzani PL, Viviani S, Anastasia A, et al. Brentuximab vedotin in relapsed/refractory Hodgkin's lymphoma: the Italian experience and results of its use in daily clinical practice outside clinical trials. Haematologica. 2013;98(8):1232–1236. doi:10.3324/haematol.2012.083048

[25] Sasse S, Rothe A, Goergen H, et al. Brentuximab vedotin (SGN-35) in patients with transplant-naive relapsed/refractory Hodgkin lymphoma. Leuk Lymphoma. 2013;54(10):2144–2148. doi:10.3109/10428194.2013.775434

[26] Gopal AK, Bartlett NL, Forero-Torres A, et al. Brentuximab vedotin in patients aged 60 years or older with relapsed or refractory CD30-positive lymphomas: a retrospective evaluation of safety and efficacy. Leuk Lymphoma. 2014;55(10):2328–2334. doi:10.3109/10428194.2013.876496

[27] Armand P, Shipp MA, Ribrag V, et al. Programmed death-1 blockade with pembrolizumab in patients with classical Hodgkin lymphoma after brentuximab vedotin failure. J Clin Oncol. 2016;34(31):3733–3739. doi:10.1200/JCO.2016.67.3467

[28] Moskowitz CH, Walewski J, Nademanee A, et al. Five-year PFS from the AETHERA trial of brentuximab vedotin for Hodgkin lymphoma at high risk of progression or relapse. Blood. 2018;132(25):2639–2642. doi:10.1182/blood-2018-07-861641

[29] Allen PB, Lu X, Chen Q, et al. Sequential pembrolizumab and AVD are highly effective at any PD-L1 expression level in untreated Hodgkin lymphoma. Blood Adv. 2023;7(12):2670–2676. doi:10.1182/bloodadvances.2022008116

[30] Johnson NA, Lavie D, Borchmann P, et al. Favezelimab (anti–LAG-3) plus pembrolizumab in patients with anti–PD-1–naive relapsed or refractory (R/R) classical Hodgkin lymphoma (cHL): an open-label phase 1/2 study. J Clin Oncol. 2022;40(16_suppl):7516. doi:10.1200/JCO.2022.40.16_suppl.7516

[31] Timmerman J, Lavie D, Johnson NA, et al. Favezelimab (anti–LAG-3) plus pembrolizumab in patients with relapsed or refractory (R/R) classical Hodgkin lymphoma (cHL) after anti–PD-1 treatment: an open-label phase 1/2 study. J Clin Oncol. 2022;40(16_suppl):7545. doi:10.1200/JCO.2022.40.16_suppl.7545

[32] Burton C, Allen P, Herrera AF. Paradigm shifts in Hodgkin lymphoma treatment: from frontline therapies to relapsed disease. Am Soc Clin Oncol Educ Book. 2024;44(3):e433502. doi:10.1200/edbk_433502

[33] Herrera AF, LeBlanc M, Castellino SM, et al. Nivolumab + AVD in advanced-stage classic Hodgkin's lymphoma. N Engl J Med. 2024;391(15):1379–1389. doi:10.1056/NEJMoa2405888