

# Addition of chemotherapy to nivolumab after PD-1 inhibitor failure as bridge to allogeneic stem cell transplantation in classical Hodgkin's lymphoma: report on three cases and literature review

Samuel Romero , Aitana Balaguer-Roselló, Juan Montoro, Paola Beneit, Amelia Martínez, Cristina Ruiz, Rafael Andreu, Manuel Guerreiro, Mario Arnao, Alberto Montava, Ana I. Vicente, Isidro Jarque and Jaime Sanz

**Abstract:** The poor prognosis of refractory or relapsed (R/R) classical Hodgkin's lymphoma (cHL) after autologous stem cell transplantation has improved greatly due to the introduction of brentuximab vedotin and PD-1 inhibitors. However, the duration of response achieved with these novel agents is too short. The information about the management of patients after anti-PD-1 therapy failure is very limited in cHL, although chemotherapy alone or combined with PD-1 inhibitors has shown encouraging results. We report three cases of heavily pretreated cHL, refractory to nivolumab monotherapy, successfully rescued with the addition of chemotherapy to nivolumab, as a bridge to allogeneic stem cell transplantation (allo-SCT). All three patients presented poor clinical features such as three to four previous lines including brentuximab vedotin and autologous stem cell transplantation, refractoriness to the last line of therapy previous to nivolumab, and rapid disease progression. Notwithstanding these characteristics and nivolumab failure, they achieved a complete response after the addition of chemotherapy, were consolidated with allo-SCT, and still remain in complete response. There are few studies concerning the combination of PD-1 inhibitors and chemotherapy after nivolumab failure, including one retrospective study and one phase II trial with nivolumab plus bendamustine. Therefore, only few patients are consolidated with allo-SCT. However, there are several ongoing trials investigating new combinations of chemotherapy and PD-1 inhibitors in R/R cHL, as well as in first line. All these data suggest that anti-PD-1 therapy may reprogram the immune system, activating and inhibiting effector and immunosuppressive cells, respectively, leading to overtake of chemorefractoriness. Allo-SCT can increase the immune-related events of patients treated with anti-PD-1 previously, consistent on acute graft-versus-host disease, sinusoidal obstruction syndrome, and noninfectious febrile syndrome. In conclusion, the combination of PD-1 inhibitor and chemotherapy may be a feasible therapy after anti-PD-1 treatment failure as a bridge to allo-SCT.

**Keywords:** allogeneic stem cell transplantation, Hodgkin's lymphoma, immune-related events, PD-1 inhibitor

Received: 17 March 2021; revised manuscript accepted: 19 July 2021.

## Introduction

Treatment landscape in relapsed or refractory (R/R) classical Hodgkin's lymphoma (cHL) has

markedly improved in the last few years due to the introduction of new targeted therapies, such as the anti-CD30 antibody-drug conjugated

*Ther Adv Hematol*

2021, Vol. 12: 1–7

DOI: 10.1177/  
20406207211038181

© The Author(s), 2021.  
Article reuse guidelines:  
[sagepub.com/journals-](https://sagepub.com/journals-permissions)  
[permissions](https://sagepub.com/journals-permissions)

Correspondence to:

**Samuel Romero**  
Hematology Department,  
Hospital Universitari i  
Politécnic La Fe, Avda.  
Fernando Abril Martorell,  
106, 46026 Valencia, Spain  
Instituto de Investigación  
Sanitaria La Fe (IIS-La Fe),  
Valencia, Spain  
[romero\\_sam@gva.es](mailto:romero_sam@gva.es)

**Aitana Balaguer-Roselló**  
**Juan Montoro**  
Hematology Department,  
Hospital Universitari i  
Politécnic La Fe, Valencia,  
Spain  
Instituto de Investigación  
Sanitaria La Fe (IIS-La Fe),  
Valencia, Spain

**Paola Beneit**  
Hematology Department,  
Hospital Universitario San  
Juan de Alicante, Spain

**Amelia Martínez**  
Hematology Department,  
Hospital Universitario de  
Torrevieja, Spain  
**Cristina Ruiz**  
Nuclear Medicine  
Department, Hospital  
Universitari i Politécnic La  
Fe, Valencia, Spain

**Rafael Andreu**  
Hematology Department,  
Hospital Universitari i  
Politécnic La Fe, Valencia,  
Spain

**Manuel Guerreiro**  
Hematology Department,  
Hospital Universitari i  
Politécnic La Fe, Valencia,  
Spain  
Instituto de Investigación  
Sanitaria La Fe (IIS-La Fe),  
Valencia, Spain

**Mario Arnao**  
**Alberto Montava**  
**Ana I. Vicente**  
Hematology Department,  
Hospital Universitari i  
Politécnic La Fe, Valencia,  
Spain

**Isidro Jarque**  
**Jaime Sanz**  
Hematology Department,  
Hospital Universitari i  
Politécnic La Fe, Valencia,  
Spain  
CIBERONC, Instituto  
Carlos III, Madrid, Spain

brentuximab vedotin (BV) and the programmed death-1 (PD-1) inhibitors.

Patients with R/R cHL after several lines of chemotherapy (CT) have historically had a dismal prognosis, especially after autologous stem cell transplantation (ASCT),<sup>1</sup> with allogeneic stem cell transplantation (allo-SCT) being the only curative approach in eligible patients.<sup>2,3</sup> However, the availability of BV first, and PD-1 inhibitors later, has allowed to rescue R/R cHL patients with objective response rates (ORRs) ranging from 69% to 75%, but with short duration of response slightly over 1 year.<sup>4-6</sup>

Unfortunately, there is scarce information about the management of patients failing to anti-PD-1 therapy, especially as bridging to allo-SCT. CT alone or in combination with PD-1 inhibitors has shown encouraging responses in some patients.<sup>7,8</sup> Radiotherapy has also been useful due to the potential synergism with PD-1 inhibitors and the abscopal effect.<sup>9</sup>

Here, we present three patients with cHL refractory to single agent nivolumab and treated with a combined approach, consisting of adding CT to nivolumab as a bridge to allo-SCT. The Institutional Review Board of University and Polytechnic Hospital La Fe approved the study (approval number: 2020/0092/EO), and written informed consent was obtained from all three patients.

### Case report

#### Case 1

A 19-year-old woman with a nodular sclerosis cHL stage II-B refractory to adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) achieved complete response (CR) after a second line with ifosfamide, carboplatin, etoposide (ICE) regimen and ASCT. Unfortunately, she relapsed after nine doses of BV maintenance after ASCT at 1.8 mg/kg every 3 weeks; it was well tolerated without relevant toxicity and dose reduction. Third line was initiated with nivolumab 3 mg/kg every 2 weeks when she was 20 years old. After six cycles, positron emission tomography/computed tomography (PET/CT) scan showed an undetermined response and she continued with additional cycles. After the ninth cycle, she developed pruritus. At that point, a combined strategy was initiated adding bendamustine at a dose of 90 mg/m<sup>2</sup> on days 1 and

2 of 21-day cycle. After two doses of nivolumab-bendamustine, she achieved partial response (PR), and the final PET/CT evaluation after six cycles was CR with resolution of the pruritus. No toxicities were seen. She underwent bone marrow reduced intensity allo-SCT from her haploidentical mother, conditioned with busulfan, fludarabine, and cyclophosphamide, using post-transplant cyclophosphamide (PTCY) in combination with sirolimus and mycophenolate mofetil as graft-versus-host disease (GVHD) prophylaxis. One month after allo-SCT, she developed acute graft-versus-host disease (aGVHD) global grade II (skin 1, gastrointestinal 1, liver 0) that completely resolved with oral steroids. Furthermore, during post-transplant recovery she presented a noninfectious febrile episode. No chronic GVHD (cGVHD) was observed. The patient is still alive in CR at 27 months after allo-SCT.

#### Case 2

A 35-year-old man diagnosed with nodular sclerosis cHL stage IV-A with pulmonary involvement was refractory to first-line therapy with ABVD plus radiotherapy. He achieved a PR after rescue therapy with etoposide, methylprednisolone, high-dose cytarabine, cisplatin (ESHAP) and consolidation with ASCT. BV maintenance was planned at standard dose, but after the second cycle disease progression occurred and BV-bendamustine combination was started for a total of four cycles, without achieving response. At that time, the patient was 37 years old and nivolumab monotherapy was initiated as the fourth line of treatment at a dose of 3 mg/kg every 2 weeks, but he progressed after six cycles. Because of the refractoriness to bendamustine and based on the preliminary results of nivolumab-ICE regimen,<sup>10</sup> he received two cycles of this drug combination achieving CR in the PET/CT scan. During nivolumab monotherapy, the patient developed a mild infusion reaction and neutropenia grade 3. With the addition of ICE, he presented grade 4 cytopenias and febrile neutropenia. He subsequently underwent peripheral blood haploidentical reduced intensity conditioning allo-SCT from his mother. The conditioning regimen was busulfan, fludarabine, and thiotepea, and the same GVHD prophylaxis as case 1 was used. Complications during the immediate post-transplant period included a noninfectious syndrome, an aGVHD global grade II (skin 3, gastrointestinal 0, liver 0) that resolved with systemic corticosteroids, and a late-onset (at day 28 of allo-SCT) mild

hepatic sinusoidal obstruction syndrome (SOS) successfully managed with supportive therapy. At day 133 after transplant, he developed moderate cGVHD (liver grade 2) managed with reintroduction of sirolimus. After 8 months of allo-SCT, he is still in CR.

### Case 3

A 30-year-old man was diagnosed with mixed cellularity cHL stage II-A. He was initially treated with ABVD achieving a CR. Five years later, he relapsed and was retreated with ABVD plus ASCT, obtaining a CR again for 18 years. A second relapse was confirmed, and third line ifosfamide, gemcitabine, vinorelbine (IGEV) treatment was given without response. BV-bendamustine was initiated (dose of BV 1.8mg/m<sup>2</sup> every 21 days), and after two cycles he achieved a PR but progressed thereafter. At that point, a fifth line with nivolumab at a fixed dose of 200mg every 2 weeks was started when the patient was 53 years old, achieving an undetermined response after four cycles and progressing after four additional cycles. He was treated with the combination nivolumab-ICE, obtaining a CR in the PET/CT scan after three cycles. During nivolumab monotherapy and nivolumab-ICE, the patient developed grade 3 and 4 hematological toxicity, respectively. This patient underwent a peripheral blood haploidentical reduced intensity allo-SCT from his son with the same conditioning, and GVHD prophylaxis regimen as case 1. After transplant, he developed global grade II aGVHD (skin 3, gastrointestinal 0, liver 0) that responded to systemic steroids. At day 147 after allo-SCT, he developed an oral mild (grade 1) cGVHD without need for systemic treatment. He remains in CR after 7 months of allo-SCT (Table 1).

### Discussion

We report here on three heavily pretreated patients with cHL, failing to nivolumab monotherapy but being successfully rescued with the addition of CT to nivolumab and subsequently consolidated with allo-SCT. Noteworthy are the poor prognosis features in all cases before initiating anti-PD-1 therapy: they were patients with three to four previous lines including BV and ASCT and refractory to the last line of treatment with a rapid disease progression. Despite these poor clinical characteristics and the subsequent

failure to nivolumab monotherapy, all three patients achieved a CR with the addition of CT and remained disease-free after allo-SCT consolidation, without relevant additional toxicity.

There is scarce information in the literature about simultaneous treatment with CT and PD-1 inhibitor in cHL. Rossi and colleagues<sup>7</sup> retrospectively analyzed 30 patients who failed anti-PD-1 monotherapy. Eleven (37%) out of 30 patients were treated with a combination of CT and PD-1 inhibitor, and the remaining 19 cases with a sequential approach. Overall, two-thirds of patients with progressive disease after PD-1 blocker obtained an objective response after the next therapy. In addition, only three patients treated with the combined approach were consolidated successfully with allo-SCT. In a prospective phase II trial, Lepik and colleagues<sup>8</sup> treated 30 patients with nivolumab plus bendamustine after nivolumab monotherapy failure, obtaining an overall response and CR rates of 87% and 57%, respectively. Interestingly, nine patients (30%) had been previously refractory to bendamustine. Five patients were consolidated with allo-SCT. Another prospective phase II trial with a combination of low-dose decitabine and camrelizumab has shown high CR rate (70%) in anti-PD-1-naïve patients and an ORR of 52% in subjects previously treated with anti-PD-1 therapy.<sup>11</sup> Furthermore, there are some ongoing clinical trials investigating the role of the addition of CT to anti-PD-1 treatment in R/R cHL, as nivolumab plus ICE escalation approach and pembrolizumab plus vorinostat.<sup>10,12</sup> On the contrary, combinations or sequential schedules of CT and PD-1 inhibitor are being tested in early phases of the disease as nivolumab or pembrolizumab plus AVD in first line.<sup>13-15</sup>

Our three patients were treated with a CT schedule not used previously, and one might speculate that the tumor response is due to CT and not related to the immunomodulatory effect of nivolumab. However, the aforementioned studies suggest that treatment with PD-1 inhibitors may reset the immune balance by resensitizing the tumor microenvironment to CT and thus allowing the immune system to overtake chemorefractoriness, which is in accordance with our observations. Furthermore, a recent retrospective study that included 81 patients failing anti-PD-1 therapy and receiving a subsequent line of treatment further supports this

Table 1. Patient characteristics.

Feature	Case 1	Case 2	Case 3
Diagnosis of cHL			
cHL diagnosis date	May 2016	August 2017	1996
Age at diagnosis of cHL (years)	19	35	30
Sex	Female	Male	Male
Primary refractory	Yes	Yes	No
BV therapy			
Treatment schedule (BV dose and interval)	BV ×9 (1.8 mg/kg every 3 weeks)	BV ×2 (1.8 mg/kg every 3 weeks) BV-Bendamustine ×4 (1.8 mg/kg and 90 mg/m <sup>2</sup> at days 1 and 2 every 21 days)	BV-Bendamustine ×4 (1.8 mg/kg and 90 mg/m <sup>2</sup> at days 1 and 2 every 21 days)
Start date	May 2017 (day + 54 ASCT)	November 2018 (day + 52 ASCT)	May 2019
BV failure date	November 2017	August 2019	August 2019
Pre-nivolumab characteristics			
Number of prior lines <sup>a</sup>	3	4	4
Last response	Progression	Without metabolic response	Progression
Last response date	November 2017	August 2019	August 2019
Ann-Arbor stage	III	IV	III
B symptoms	No	No	No
Bulky disease	No	No	No
Extranodal involvement	No	Yes	No
Nivolumab therapy			
Start date	November 2017	September 2019	August 2019
Age at nivolumab start (years)	20	37	53
Nivolumab dose and interval	3 mg/kg, every 2 weeks	3 mg/kg, every 2 weeks	200 mg, every 2 weeks
Number of cycles	9	6	8
Nivolumab failure date	April 2018	December 2019	December 2019
CT schedule combined	Bendamustine	ICE	ICE
Number of cycles	6	2	3
CR CT-nivolumab date	August 2018	February 2020	April 2020
Allo-SCT data			
Allo-SCT date	September 2018	April 2020	May 2020
Age at allo-SCT	21	38	54
Type of donor	Haploidentical, mother	Haploidentical, mother	Haploidentical, son

(continued)

**Table 1.** (continued)

Feature	Case 1	Case 2	Case 3
Age of donor	46	64	18
Source of stem cells	Bone marrow	Peripheral blood	Peripheral blood
Number of CD34 cells infused	1.42 × 10 <sup>6</sup> /kg	5.64 × 10 <sup>6</sup> /kg	9.82 × 10 <sup>6</sup> /kg
Conditioning regimen	RIC, Bu-Flu-Cy	RIC, Bu-Flu-TT	RIC, Bu-Flu-Cy
GVHD prophylaxis	PTCY, sirolimus, MMF	PTCY, sirolimus, MMF	PTCY, sirolimus, MMF
Days from the last dose of nivolumab to allo-SCT	59	72	43
aGVHD	Yes	Yes	Yes
Stage and organ involvement of aGVHD	Global grade II (skin 1, gastrointestinal 1, liver 0)	Global grade II (skin 3, gastrointestinal 0, liver 0)	Global grade II (skin 3, gastrointestinal 0, liver 0)
Corticosteroids aGVHD treatment and response	2 mg/kg/day oral, complete response	2 mg/kg/day oral, complete response	1 mg/kg/day oral, complete response
SOS	No	Yes	No
Noninfectious febrile syndrome	Yes	Yes	No
cGVHD	No	Yes, moderate (liver grade 2)	Yes, mild (oral grade 1)
Last follow-up (months after allo-SCT) and response	27, CR	8, CR	7, CR

aGVHD, acute GVHD; allo-SCT, allogeneic stem cell transplantation; ASCT, autologous stem cell transplantation; Bu, busulfan; BV, brentuximab vedotin; cGVHD, chronic GVHD; cHL, classical Hodgkin's lymphoma; CR, complete response; CT, chemotherapy; Cy, cyclophosphamide; Flu, fludarabine; GVHD, graft-versus-host disease; MMF, micophenolate mofetil; PTCY, post-transplant cyclophosphamide; RIC, reduced intensity conditioning; SOS, sinusoidal obstruction syndrome; TT, thiotepa.  
<sup>a</sup>BV maintenance has been considered as an individual line (Table 1).

concept. PD-1 inhibitors improved the duration of response to the next therapy (169 days) compared with the most recent prior treatment before PD-1 blocker (84 days).<sup>16</sup> PD-1 inhibitors and CT are believed to act synergistically and bidirectionally: on one side, PD-1 inhibitors remove the 'brakes' on T-cell immune responses and induce changes into tumor microenvironment by impairing the function of immunosuppressive cells. This combinatory effect allows tumor cells to become more sensitive not only to immunogenic cell death but also to direct DNA damage of several CT. On the other side, although CT can diminish the total number of immune cells, it enhances the antitumor activity of PD-1 blockers through the selective activation of effectors cells (T-helper type 1 cells, cytotoxic T-lymphocytes,  $\gamma/\delta$  T-cells, and dendritic cells) and the repression of immunosuppressive cells (regulatory T-cells and myeloid-derived suppressor cells).

This synergetic effect has been further explained by the influence of PD-1 inhibitors on several immunologic signaling pathways and surface molecules implicated in the cHL clinical course (such as STAT6, HLA I, or PD-L2).<sup>16-19</sup>

Allo-SCT has a relevant role as consolidation therapy for R/R cHL, but it is still controversial whether previous anti-PD-1 therapy can increase the risk of immune-mediated events after allo-SCT, like GVHD, as seen in murine models.<sup>20</sup> The Spanish group GELTAMO reported its experience in the treatment of R/R cHL with nivolumab in a series of 74 cases.<sup>21</sup> In these report, 39 patients (52%) underwent allo-SCT, showing a rate of grade II-IV aGVHD, SOS, and noninfectious febrile syndrome of 33%, 8%, and 36%, respectively. Recently, Merryman and colleagues<sup>22</sup> have reported the largest series (209 cases) of R/R cHL patients treated

with anti-PD-1 therapy before allo-SCT. The cumulative incidence of aGVHD for any grade, grades II–IV, and grades III–IV was 54%, 37%, and 15%, respectively, and 34% for cGVHD. Interestingly, a shorter interval from the last dose of PD-1 inhibitor to allo-SCT (<80 days) was associated with a higher risk of aGVHD. The use of PTCY as GVHD prophylaxis did not decrease the risk of aGVHD, although it reduced the rate of cGVHD. Regarding SOS and noninfectious febrile syndrome, the cumulative incidence was 3% and 23%, respectively. These immune-mediated post-transplant complications have been reported in other small series.<sup>23,24</sup> There is little information about the rate of immune-related events in patients receiving PD-1 inhibitors plus CT. Regarding our three patients, all of them developed immune-related events but were successfully managed in every case. They presented grade II aGVHD, one mild SOS, and two noninfectious febrile syndrome. However, all of them received an allo-SCT from haploidentical donors, which is a well-known risk factor for developing GVHD.<sup>25</sup>

Despite our success in the management of these patients before allo-SCT, we are aware that these findings are based on individual cases, reflecting the need for clinical trials designed to study R/R cHL patients refractory to PD-1 inhibitors. Similarly, we are unable to establish whether the combination of anti-PD-1 therapy with CT can modify the rate of immune-mediated events after allo-SCT due to the reduced number of patients. However, and despite the limited information available, the concomitant approach of PD-1 inhibitor and CT may be a feasible option after anti-PD-1 treatment failure, with an acceptable toxicity profile, as bridge to allo-SCT.

#### Author contributions

SR and ABR designed the study. SR, ABR, JM, and MG performed the research. JM, PB, AM, CR, RA, MA, AIV, and AM were the treating physicians and collected data on patients. SR, ABR, MG, IJ, and JS wrote the paper. All authors gave final approval to the manuscript.

#### Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

#### Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

#### ORCID iD

Samuel Romero  <https://orcid.org/0000-0002-1060-2158>

#### References

1. Moskowitz AJ, Perales MA, Kewalramani T, *et al.* Outcomes for patients who fail high dose chemoradiotherapy and autologous stem cell rescue for relapsed and primary refractory Hodgkin lymphoma. *Br J Haematol* 2009; 146: 158–163.
2. Piñana JL, Sanz J, Esquirol A, *et al.* Umbilical cord blood transplantation in adults with advanced Hodgkin's disease: high incidence of post-transplant lymphoproliferative disease. *Eur J Haematol* 2016; 96: 128–135.
3. Sureda A, Stavrik SG, Boumendil A, *et al.* Changes in patients population and characteristics of hematopoietic stem cell transplantation for relapsed/refractory Hodgkin lymphoma: an analysis of the Lymphoma Working Party of the EBMT. *Bone Marrow Transplant* 2020; 55: 2170–2179.
4. Chen R, Gopal AK, Smith SE, *et al.* Five-year survival and durability results of brentuximab vedotin in patients with relapsed or refractory Hodgkin lymphoma. *Blood* 2016; 128: 1562–1566.
5. 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: 1428–1439.
6. Chen R, Zinzani PL, Lee HJ, *et al.* Pembrolizumab in relapsed or refractory Hodgkin lymphoma: 2-year follow-up of KEYNOTE-087. *Blood* 2019; 134: 1144–1153.
7. Rossi C, Gilhodes J, Maerevoet M, *et al.* Efficacy of chemotherapy or chemo-anti-PD-1 combination after failed anti-PD-1 therapy for relapsed and refractory Hodgkin lymphoma: a series from Lysa centers. *Am J Hematol*. Epub ahead of print 8 June 2018. DOI: 10.1002/ajh.25154.

8. Lepik KV, Mikhailova NB, Kondakova EV, *et al.* A study of safety and efficacy of nivolumab and bendamustine (NB) in patients with relapsed/refractory Hodgkin lymphoma after nivolumab monotherapy failure. *Hemasphere* 2020; 4: e401.
9. Baues C, Trommer-Nestler M, Jablonska K, *et al.* Short review of potential synergies of immune checkpoint inhibition and radiotherapy with a focus on Hodgkin lymphoma: radio-immunotherapy opens new doors. *Immunotherapy* 2017; 9: 423–433.
10. Herrera AF, Chen RW, Palmer J, *et al.* PET-adapted nivolumab or nivolumab plus ICE as first salvage therapy in relapsed or refractory Hodgkin lymphoma. *Blood* 2019; 134(Supplement\_1): 239.
11. Nie J, Wang C, Liu Y, *et al.* Addition of low-dose decitabine to anti-PD-1 antibody camrelizumab in relapsed/refractory classical Hodgkin lymphoma. *J Clin Oncol* 2019; 37: 1479–1489.
12. Herrera AF, Chen L, Popplewell LL, *et al.* Preliminary results from a phase I trial of pembrolizumab plus vorinostat in patients with relapsed or refractory diffuse large B-cell lymphoma, follicular lymphoma, and Hodgkin lymphoma. *Blood* 2019; 134(Supplement\_1): 759.
13. Ramchandren R, Domingo-Domènech E, Rueda A, *et al.* Nivolumab for newly diagnosed advanced-stage classic Hodgkin lymphoma: safety and efficacy in the phase II Checkmate 205 Study. *J Clin Oncol* 2019; 37: 1997–2007.
14. Bröckelmann PJ, Goergen H, Keller U, *et al.* Efficacy of nivolumab and AVD in early-stage unfavourable classic Hodgkin lymphoma: the randomized phase 2 German Hodgkin Study Group NIVAHL Trial. *JAMA Oncol* 2020; 6: 1–9.
15. Allen PB, Savas H, Evens AM, *et al.* Pembrolizumab followed by AVD in untreated early unfavourable stage classical Hodgkin lymphoma. *Blood*. Epub ahead of print 29 September 2020. DOI: 10.1182/blood.20200007400.
16. Carreau NA, Pail O, Armand P, *et al.* Checkpoint blockade treatment may sensitize Hodgkin lymphoma to subsequent therapy. *Oncologist* 2020; 25: 878–885.
17. Galluzzi L, Senovilla L, Zitvogel L, *et al.* The secret ally: immunostimulation by anticancer drugs. *Nat Rev Drug Discov* 2012; 11: 215–233.
18. Galluzzi L, Zitvogel L and Kroemer G. Immunological mechanisms underneath the efficacy of cancer therapy. *Cancer Immunol Res* 2016; 4: 895–902.
19. Cubas R, Moskalenko M, Cheung J, *et al.* Chemotherapy combines effectively with anti-PD-L1 treatment and can augment antitumor responses. *J Immunol* 2018; 201: 2273–2286.
20. Herbaux C, Gauthier J, Brice P, *et al.* Efficacy and tolerability of nivolumab after allogeneic transplantation for relapsed Hodgkin lymphoma. *Blood* 2017; 129: 2471–2478.
21. Martínez C, Carpio C, Heras I, *et al.* Potential survival benefit for patients receiving allogeneic hematopoietic stem cell transplantation after nivolumab therapy for relapsed/refractory Hodgkin lymphoma: real-life experience in Spain. *Biol Blood Marrow Transplant* 2020; 26: 1534–1542.
22. Merryman RW, Castagna L, Giordano L, *et al.* Allogeneic transplantation after PD-1 blockade for classic Hodgkin lymphoma. *Leukemia*. Epub ahead of print 3 March 2021. DOI: 10.1038/s41375-021-01193-6.
23. Ijaz A, Khan AY, Malik SU, *et al.* Significant risk of graft-versus-host-disease with exposure to checkpoint inhibitors before and after allogeneic transplantation. *Biol Blood Marrow Transplant* 2019; 25: 94–99.
24. Dada R and Usman B. Allogeneic hematopoietic stem cell transplantation in r/r Hodgkin lymphoma after treatment with checkpoint inhibitors: feasibility and safety. *Eur J Haematol* 2019; 102: 150–156.
25. Montoro J, Piñana JL, Hernández-Boluda JC, *et al.* Uniform graft-versus-host disease prophylaxis with posttransplant cyclophosphamide, sirolimus, and mycophenolate mofetil following hematopoietic stem cell transplantation from haploidentical, matched sibling and unrelated donors. *Bone Marrow Transplant* 2020; 55: 2147–2159.

Visit SAGE journals online  
journals.sagepub.com/  
home/tah

 SAGE journals