blood advances

TO THE EDITOR:

GVHD in the era of checkpoint inhibition in Hodgkin lymphoma

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Allogeneic hematopoietic cell transplantation (alloHCT) remains a potential curative option for patients with relapse/refractory (R/R) Hodgkin lymphoma (HL).[1,2] The effective bridge to alloHCT with immune checkpoint inhibitors (ICIs) is known to be associated with increased transplant morbidity and mortality.[3,4]

We have read with great interest the article by Tabbara et al[5] that established a 5-year 91% survival rate in the setting of R/R HL among patients who received ICIs before alloHCT. The excess graft-versus-host disease (GVHD) risk reported in the study was mostly observed in ICI-exposed patients with a duration of post-HCT immunosuppression (IS) of ≤60 days.[5]

We therefore analyzed a cohort of 5 patients with R/R HL who were treated at our center with ICI, followed by alloHCT, from 2017 (see figure). At the time of alloHCT, the median patient age was 32 years (range, 30-52); 4 of them were in complete remission, whereas 1 was in partial remission after a median of 6 cycles of ICIs (range, 3-8). We observed only 1 case of overlap GVHD (20%), classified as acute grade 2[6] and moderate chronic,[7] at around 30 days after transplant in the only patient who did not receive posttransplant cyclophosphamide (PTCy) and who had the shortest washout period between ICI and alloHCT (48 days vs a median of 67 days). GVHD treatment was based on multiple IS agents, namely steroids, mycophenolate mofetil, pentostatin, sirolimus, and photopheresis. All other patients received PTCy regardless of the donor type. The bone marrow was the stem cell source in 2 of 5 patients; all but 1 received a transplant from a matched unrelated donor. The median duration of IS was 123 days (range, 108-393). All patients were alive and disease free at the last follow-up (median follow-up 256 days [range, 47-2400]).

In conclusion, our study on a small but contemporary cohort of patients with R/R HL supports the fundamentals of the current strategy in this setting, namely pretransplant ICI washout period, in vivo T-cell depletion, and length of IS, which improved patient outcomes and mitigated toxicity. In support of previous reports, PTCy improved GVHD incidence in our cohort.[2,8]

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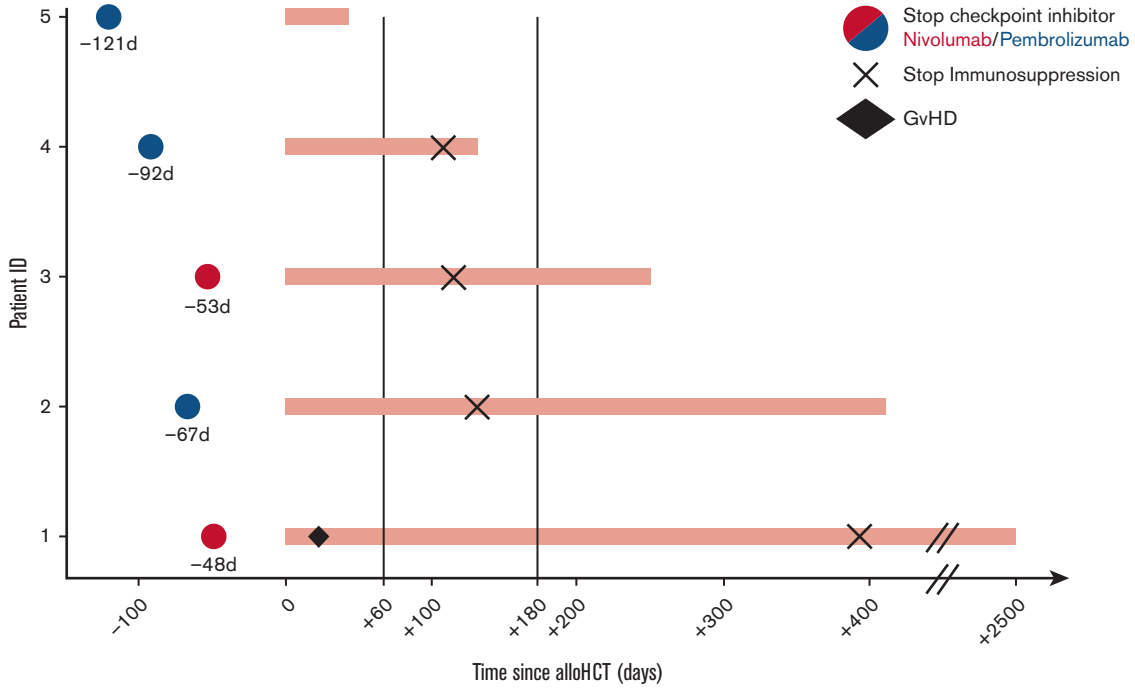
Patient ID	Prior treatments (no.)	ICI as last therapy before alloHCT	Donor	Allograft source	Conditioning	GvHD prophylaxis	Chimerism at day +60
1	6	Yes	MUD 10/10	PBSC	Thio-CTX-Flu	ATG/CyA/MTX	≥ 95% D
2	4	Yes	MUD 10/10	BM	CTX-Flu-TBI2Gy	PTCY/CyA/MMF	≥ 95% D
3	4	Yes	MUD 10/10	BM	CTX-Flu-TBI2Gy	PTCY/CyA/MMF	≥ 95% D
4	5	No*	MRD 10/10	PBSC	CTX-Flu-TBI2Gy	PTCY/CyA/MMF	≥ 95% D
5	4	No*	MUD 10/10	PBSC	CTX-Flu-TBI2Gy	PTCY/CyA/MMF	NR



AlloHCT characteristics, ICI before HCT, IS after HCT, and GVHD in 5 patients with R/R HL. Each bar represents 1 single patient in the study. Time 0 was defined as the day of alloHCT, with critical time points being the day of discontinuation of ICI, IS (CyA), or the occurrence of GVHD. Patients' transplant characteristics are illustrated in the upper part of the figure. *The 2 patients who underwent another line of therapy after ICI as a bridge to transplant were both treated with 2 cycles of BeGEV chemotherapy. GVHD prophylaxis included the following: ATG 2.5 mg/kg on days −4 and −3; CyA, 3 mg/kg IV from day +5; MMF, 15 mg/kg thrice daily between days +5 and +35; MTX, 15 mg/m^2 on day +1 and 10 mg/m^2 on days +3 and +6; and PTCy, 40 mg/kg IV on days +3 and +4. Conditioning regimens were as follows: CTX-Flu-TBI2Gy, CTX 14.5 mg/kg IV on days −6 and −5 with Flu 30 mg/m^2 IV on days −6 through −2 and TBI as a single fraction at a dose of 2 Gy on day −1; and Thio-CTX-Flu, Thio 6 mg/kg IV twice daily on day −5 with CTX 30 mg/kg IV on days −4 and −3 and Flu 30 mg/m^2 IV on days −4 and −3. ATG, antithymocyte globulin; BeGEV, bendamustine, gemcitabine, vinorelbine; BM, bone marrow; CTX, cyclophosphamide; CyA, cyclosporine; D, donor; Flu, fludarabine; MMF, mycophenolate mofetil; MRD, matched-related donor; MTX, methotrexate; MUD, matched unrelated donor; NR, not reached; PBSC, peripheral blood stem cell; TBI, total body irradiation; Thio, thiotepa.

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