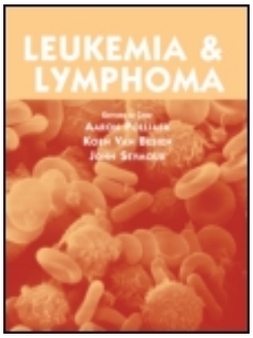

Leukemia & Lymphoma

ISSN: 1042-8194 (Print) 1029-2403 (Online) Journal homepage: https://www.tandfonline.com/loi/ilal20

Brentuximab vedotin: the science of common sense

Matthew A. Lunning & Anas Younes

To cite this article: Matthew A. Lunning & Anas Younes (2013) Brentuximab vedotin: the science of common sense, Leukemia & Lymphoma, 54:10, 2089-2090, DOI: 10.3109/10428194.2013.786074

To link to this article: https://doi.org/10.3109/10428194.2013.786074

View supplementary material

Accepted author version posted online: 21 Mar 2013.
Published online: 30 Apr 2013.

Submit your article to this journal

Article views: 916

View related articles

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=ilal20

Leukemia & Lymphoma, October 2013; 54(10): 2089–2090
© 2013 Informa UK, Ltd.
ISSN: 1042-8194 print / 1029-2403 online
DOI: 10.3109/10428194.2013.786074

informa
healthcare

COMMENTARY

Brentuximab vedotin: the science of common sense

Matthew A. Lunning & Anas Younes

Memorial Sloan-Kettering Cancer Center, New York, NY, USA

An estimated 15–30% of patients will experience either primary refractory or a relapse of Hodgkin lymphoma (HL) despite modern therapy [1]. A second chance at cure can be achieved using non-cross-resistant second-line therapy followed by high-dose therapy and autologous stem cell transplant [2]. Several studies have demonstrated that tumor chemosensitivity predicts better treatment outcome after stem cell transplant, with the best outcome observed in patients who achieve a positron emission tomography-negative response [3]. In general, patients who do not respond to second-line therapy are considered not ideal candidates for stem cell transplant, and typically are offered subsequent treatments. Novel therapies to improve response rates and the quality of remissions in patients with relapsed and refractory HL would increase the pool of transplant-eligible patients, and therefore the chances of cure.

Brentuximab vedotin is an anti-CD30 drug–antibody conjugate that delivers a potent tubulin-disrupting agent to the malignant Hodgkin and Reed–Sternberg (HRS) cells of HL. The initial phase I clinical trial examined the safety and efficacy of brentuximab vedotin in heavily pretreated patients [4]. In a follow-up phase II study that led to the approval of brentuximab vedotin by the United States Food and Drug Administration (FDA), 102 patients with relapsed HL were treated. All patients were required to have prior stem cell transplant. The overall response rate was 75%, with 34% of patients achieving complete remissions [5]. Based on these impressive results, the FDA granted approval to patients with HL who had relapsed post-stem cell transplant. In addition, the FDA extended the approved indication to include patients who are transplant-ineligible and were refractory to two prior combination chemotherapy regimens [6]. This extended label indication was based more on common sense than on actual data. Given the high response rate and excellent safety profile in the post-transplant setting, it is logical to predict that brentuximab vedotin would be at least as effective in the pre-transplant setting.

In this edition of ***Leukemia and Lymphoma***, Sasse and colleagues expand the limited literature on transplant-naive or transplant ineligible relapsed/refractory patients with HL who have received brentuximab vedotin [7]. In total, 14 patents were treated with brentuximab vedotin in a named program at the FDA-approved dosing and schedule. Congruent with the prior phase II study, brentuximab vedotin performed well, with an overall response rate of 71% (9/14) and a complete response rate of 36% (5/14). Importantly, brentuximab vedotin allowed 56% (5/9) of patients felt to be transplant-eligible to undergo transplant. At the time of publication four are alive. Brentuximab vedotin also afforded tolerable palliative treatment, as noted by no dose reductions due to toxicity in the transplant-ineligible cohort. Other groups have also reported small numbers of patients treated in similar situations, and their results remain encouraging (Table I).

The safety and efficacy of brentuximab vedotin in combination with front-line and second-line regimens are currently being investigated in prospective trials. In a phase I trial, brentuximab vedotin combined with ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) was associated with significant pulmonary toxicity [8]. This was an unexpected toxicity and could be prevented by omitting bleomycin. Therefore, despite the excellent safety profile of single-agent brentuximab vedotin, clinicians should avoid the temptation of adding brentuximab vedotin to commonly used regimens outside of clinical trials.

The most understudied population at this point is the transplant-ineligible cohort. In this setting, the best dose and schedule, and ideal number of doses of brentuximab vedotin, remain undetermined. Likewise, several other questions in the relapsed/refractory setting remain. Is there a difference in transplant outcome in patients achieving remission after conventional chemotherapy compared with brentuximab vedotin? Is there an impact on the ability to collect stem cells or for stem cell engraftment after brentuximab vedotin? Should brentuximab vedotin be given as a single agent or in combination in the pre-transplant setting? Should the role of stem cell transplant be re-examined in the brentuximab vedotin era, similar to what has been done in non-Hodgkin lymphoma in the rituximab era? Logically, the answers to these questions can only be obtained from prospective clinical trials, some of which are being conducted.

Correspondence: Anas Younes, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, USA. E-mail: younesa@mskcc.org

This commentary accompanies an article to be published in *Leukemia & Lymphoma*. Please refer to the table of contents of the print issue in which this commentary appears.

Table I. Brentuximab vedotin in transplant-naive relapsed/refractory Hodgkin lymphoma.

Authors	Number*	Refractory†	Transplant-ineligible	ORR	CR rate	Proceeded to transplant
Sasse *et al.* [7]	14	11	5	71%	36%	56%
Forero-Torres *et al.* [9]	20	13	7	30%	10%	23%
Gibb *et al.* [10]	18	UNK	UNK	72%	17%	22%‡
Chen *et al.* [11]	8	6	UNK	88%	50%	75%

ORR, overall response rate; CR, complete responses; UNK, unknown.
*Includes only patients with Hodgkin lymphoma with evaluable response.
†Refractory to at least one therapy.
‡May include patients considered transplant-ineligible.

With the introduction of brentuximab vedotin, the first new agent to be approved for patients with HL in more than 30 years, a new era has begun for the thousands of young men and women who have relapsed and refractory non-curable HL. The study reported by Sasse *et al.* has provided valuable information to fill a knowledge gap, and they are to be congratulated for taking this initiative. For many, these clinical responses provided hope for a second chance at cure. While it is tempting to speculate that further development of brentuximab vedotin is likely to improve the cure rate of HL, it is now important to be steadfast in collecting data from prospective clinical trials to scientifically validate common-sense approaches.

Potential conflict of interest: Disclosure forms provided by the authors are available with the full text of this article at www.informahealthcare.com/lal.

References

[1] Diehl V, Franklin J, Pfreundschuh M, et al. Standard and increased-dose BEACOPP chemotherapy compared with COPP-ABVD for advanced Hodgkin's disease. N Engl J Med 2003;348:2386–2395.
[2] Majhail NS, Weisdorf DJ, Defor TE, et al. Long-term results of autologous stem cell transplantation for primary refractory or relapsed Hodgkin's lymphoma. Biol Blood Marrow Transplant 2006;12: 1065–1072.
[3] Moskowitz CH, Matasar MJ, Zelenetz AD, et al. Normalization of pre-ASCT, FDG-PET imaging with second-line, non-cross-resistant, chemotherapy programs improves event-free survival in patients with Hodgkin lymphoma. Blood 2012;119:1665–1670.
[4] Younes A, Bartlett NL, Leonard JP, et al. Brentuximab vedotin (SGN-35) for relapsed CD30-positive lymphomas. N Engl J Med 2010; 363:1812–1821.
[5] Younes A, Gopal AK, Smith SE, et al. Results of a pivotal phase II study of brentuximab vedotin for patients with relapsed or refractory Hodgkin's lymphoma. J Clin Oncol 2012;30:2183–2189.
[6] de Claro RA, McGinn K, Kwitkowski V, et al. U.S. Food and Drug Administration approval summary: brentuximab vedotin for the treatment of relapsed Hodgkin lymphoma or relapsed systemic anaplastic large-cell lymphoma. Clin Cancer Res 2012;18:5845–5849.
[7] Sasse S, Rothe A, Goergen H, et al. Brentuximab vedotin (SGN-35) in patients with transplant-naive relapsed/refractory Hodgkin lymphoma. Leuk Lymphoma 2013;54:2144–2148.
[8] Ansell SM, Connors JM, Park SI, et al. Frontline therapy with brentuximab vedotin combined with ABVD or ABD in patients with newly diagnosed advanced stage Hodgkin lymphoma. Blood 2012;120(Suppl. 1): Abstract 798.
[9] Forero-Torres A, Fanale M, Advani R, et al. Brentuximab vedotin in transplant-naive patients with relapsed or refractory hodgkin lymphoma: analysis of two phase I studies. Oncologist 2012;17: 1073–1080.
[10] Gibb A, Jones C, Bloor A, et al. Brentuximab vedotin in refractory CD30+ lymphomas: a bridge to allogeneic transplantation in approximately one quarter of patients treated on a named patient programme at a single UK centre. Haematologica 2012 Oct 12. [Epub ahead of print].
[11] Chen RW, Palmer J, Siddiqi T, et al. Brentuximab vedotin as first line salvage theapy in relapsed/refractory HL. Blood 2012; 120(Suppl. 1): Abstract 3699.