Brentuximab Vedotin in CD30-Positive Lymphomas: A SIE, SIES, and GITMO Position Paper

Pier Luigi Zinzani,1 Paolo Corradini,2 Alessandro M. Gianni,3,4 Massimo Federico,5 Armando Santoro,6 Umberto Vitolo,7 Giovanni Barosi,8 Sante Tura9

Abstract

Brentuximab vedotin (BV) is approved for the treatment of patients with relapsed or refractory CD30-positive Hodgkin lymphoma, and relapsed or refractory systemic anaplastic large-cell lymphoma. Several uncertainties remain regarding the optimal use of the drug in its approved indications as well as outside them. This article reports recommendations on the use of BV issued during a consensus project, sponsored by the Italian Society of Hematology (SIE) and its affiliate societies, Società Italiana di Ematologia Sperimentale (SIES) and Gruppo Italiano Trapianto di Midollo Osseo (GITMO). Scientific evidence on BV was evaluated by a panel of experts, and consensus was developed by group discussion for key questions selected according to the clinical relevance. The following key issues were addressed: testing CD30 positivity to assess eligibility to BV; assessing practice indications of BV in Hodgkin lymphoma and systemic anaplastic large-cell lymphoma; providing pretreatment evaluation of patients candidates to BV; monitoring the response to BV; managing patients treated with BV; and assessing the role of BV in other CD30-positive lymphomas.

Introduction

Brentuximab vedotin (BV) is an antibody—drug conjugate comprising a human CD30-directed chimeric immunoglobulin G1 antibody covalently bonded to a microtubule-disrupting agent (monomethyl auristatin E [MMAE]) by a protease-cleavable linker.1

BV is internalized after binding to CD30 surface receptors, and MMAE is released, inducing apoptosis.7 The drug has exhibited potent and specific cytotoxicity against CD30-positive cells in vitro and in vivo.7

BV has been approved in the United States, Canada, and Europe for the treatment of patients with Hodgkin lymphoma (HL) after failure of either autologous stem-cell transplantation (ASCT) or 2 or more previous multiagent chemotherapy regimens in patients who are not candidates for ASCT.2 It is also approved for the treatment of patients with systemic anaplastic large-cell lymphoma (sALCL) after failure of 1 or more previous multiagent chemotherapy regimens.2

BV has represented a major breakthrough in the treatment of CD30-positive lymphoid malignancies; however, several uncertainties still remain on the optimal use of the drug in approved indications. In addition, new questions are emerging on the use of the drug in earlier stages of HL and sALCL, as well as its effectiveness as a consolidation therapy in HL. Moreover, its role in other CD30-positive lymphoid malignancies remains to be determined.

In order to support physicians in managing patients who are candidates for BV, a consensus development conference project on
Brentuximab Vedotin in CD30-Positive Lymphomas

BV was convened under the sponsorship of the Italian Society of Hematology (SIE) and its affiliate societies, Società Italiana di Ematologia Sperimentale (SIES) and Gruppo Italiano Trapianto di Midollo Osseo (GITMO).

Design and Methods
Organization
Two chairmen (S.T. and G.B.) appointed an expert panel (EP) of 7 experts, selected for their expertise in research and clinical practice of adult lymphoid malignancies. A clinician with expertise in clinical epidemiology (G.B.) assured the methodologic correctness of the process.

Framing the Domain of Recommendations
During an initial meeting, the EP agreed on the areas of major concern in the use of BV by generating and ranking ordering clinical key questions using the criterion of clinical relevance—impact on the management of patients and risk of inappropriateness—through a Delphi process.3 The 11 candidate key questions that ranked highest formed the set of questions addressed in this article.

Consensus Process
During the first of 3 meetings, the EP examined the current state of knowledge regarding BV. Each panelist drafted statements that addressed 1 or more of the preliminarily identified key questions. Subsequently, each panelist scored his agreement with the statements made by other panelists and provided suggestions for rephrasing. For exploiting this phase of the process, the EP was convened, and 3 consensus conferences were held in Bologna, Italy. The overall goals of the meetings were to reach a definite consensus over question-specific statement for which there was disagreement during the first-round postal phase. The nominal group technique was used by which participants were first asked to comment in round-robin fashion on their preliminary votes and then to propose a new vote. If an at least 80% consensus on the statement was not achieved, the choices were discussed and a second vote taken. If an 80% consensus was still not attained, the issue was declared undecidable, and no further attempt was made.

Results
Testing CD30 Positivity to Assess Eligibility to BV
In classical HL and sALCL, CD30 positivity is present in nearly 100% of the malignant cells. Consequently, the US Food and Drug Administration (FDA) did not require a validated CD30 in vitro diagnostic test for the accelerated approval for BV in both diseases. However, other lymphoid neoplasms are much more heterogeneous as to what CD30 positivity is concerned. For instance, primary mediastinal B-cell lymphoma carries CD30 in about 85% of cases at a moderate intensity; endemic Burkitt lymphoma expresses CD30 in about 30% of patients; and diffuse large B-cell lymphoma shows positivity for CD30 in only a small proportion of cases.5,6 CD30 expression on a variety of T-cell lymphomas, including angioimmunoblastic T-cell lymphoma and peripheral T-cell lymphoma (PTCL) not otherwise specified, ranges from 0% to 64%.5,6

Documentation that CD30 protein expression in noncutaneous PTCLs was highly correlated to mRNA levels led to the conclusion that immunohistochemistry is a valuable tool in clinical practice to assess CD30 expression in CD30-expressing lymphomas.7 In the most recent clinical trials with BV in T-cell and B-cell lymphomas, responses were reported among patients with all levels of CD30 expression in their tumor samples, including patients with CD30 undetectable by immunohistochemistry.7 The EP claimed immunohistochemistry for CD30 to be a useful tool to assess this biomarker for the correlation between the target and the effect of BV.

Recommendations.
• Testing and grading CD30 reactivity in malignant tissues in order to assess the eligibility for BV is not mandatory in the drug’s approved indications (ie, refractory or relapsed HL and refractory or relapsed sALCL).
• Testing and reporting the CD30 reactivity in malignant tissues is recommended in the experimental use of the drug. In these circumstances, a standard immunostaining technique is advised.

Practice Indications of BV in HL
Refractory or Relapsed Disease. An estimated 15% to 30% of patients with HL experience either primary refractoriness or relapse despite modern therapy.2 A second chance of cure can be achieved using non-cross-resistant second-line therapy followed in responsive patients by high-dose chemotherapy and ASCT, a strategy that is curative in approximately half of those who undergo the procedure.8 However, patients whose disease does not respond to second-line therapy usually are not offered ASCT and instead are offered subsequent treatments.

The initial phase 1 clinical trial with BV examined the safety and efficacy of the drug in 45 heavily pretreated relapsed or refractory CD30-positive hematologic cancers, primarily HL.9 In a subsequent pivotal phase 2 study, in 102 patients with relapsed HL previously treated with ASCT, BV induced an overall response rate (ORR) of 75%, with 34% of patients experiencing complete response (CR).10 On the basis of these impressive results, the FDA granted approval to HL patients who had experienced relapse after ASCT.

After approval by FDA, further evidence on efficacy of BV in heavily pretreated relapsed or refractory HL was derived from patients receiving the drug through a Named Patient Program (NPP). Comparing the NPP experiences with the pivotal study,10 the ORR and CR rates ranged from 60% to 72% and from 17% to 22%, respectively (Table 1).

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>ORR (%)</th>
<th>CR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pivotal</td>
<td>102</td>
<td>75</td>
<td>34</td>
</tr>
<tr>
<td>German NPP</td>
<td>45</td>
<td>60</td>
<td>22</td>
</tr>
<tr>
<td>UK NPP</td>
<td>18</td>
<td>72</td>
<td>17</td>
</tr>
<tr>
<td>Italian NPP</td>
<td>65</td>
<td>70.7</td>
<td>21.5</td>
</tr>
<tr>
<td>French NPP</td>
<td>241</td>
<td>58</td>
<td>32</td>
</tr>
</tbody>
</table>

Abbreviations: CR = complete response; NPP = Named Patient Program; ORR = overall response rate.
Follow-up analysis of the pivotal phase 2 study documented a durable remission and favorable long-term survival. Twenty-five percent of patients with an objective response to BV remained in remission after a median follow-up of approximately 3 years.15

The FDA extended the approved indication to include patients who were ineligible for a transplant and refractory to 2 prior combination chemotherapy regimens.2 This extended-label indication, however, was based on poor evidence. In the initial phase 1 trial of the 12 patients who had not received ASCT before BV, 3 (25%) responded to BV, with 2 CR and 1 partial response (PR).9 However, the efficacy of BV in patients before transplantation was confirmed in a published retrospective analysis of 20 transplant-naive patients with HL treated with BV within two phase 1 trials: 4 of the 6 responding patients were not previously eligible for ASCT because their disease was chemorefractory.16 Another report by Sasse et al17 included 14 patients with primary progressive or relapsed HL without prior ASCT; the overall response was 71% (10 of 14), with 5 CR and 5 PR. In addition, Garcia et al18 reported an ORR of 66.6% in patients treated with BV before ASCT. Finally, in all NPP experiences, responses were reported (with several CRs) in transplant-naive relapsed or refractory HL patients.11–14 These results indicate that BV allowed proceeding to high-dose chemotherapy in some of those patients with chemotherapy-refractory HL and might finally result in overcoming their dismal prognosis.

Consolidation Therapy. The benefit of consolidation therapy with BV is the question addressed by the AETHERA trial, a randomized, double-blind, placebo-controlled, phase 3 trial at 78 sites in North America and Europe.19 Patients with unfavorable-risk relapsed or primary refractory classic HL who had undergone autologous stem-cell transplantation were randomly assigned to receive 16 cycles of 1.8 mg/kg BV (n = 165) or placebo (n = 164) intravenously every 3 weeks, starting 30 to 45 days after transplantation. Progression-free survival (PFS) by independent review was significantly improved in patients in the BV group compared to those in the placebo group (hazard ratio, 0.57; 95% confidence interval, 0.40-0.81; P = .0013). Median PFS by was 42.9 months for patients in the BV group compared to 24.1 months for those in the placebo group. The most frequent adverse events in the BV group compared to placebo were peripheral sensory neuropathy (56% vs. 16%) and neutropenia (35% vs. 12%).

BV in Combination. Several ongoing trials including HL patients with multiple relapses are investigating BV in combination with other novel drugs such as temsirolimus (NCT01902160) or ipilimumab (NCT01896999) and conventional chemotherapeutics such as bendamustine (NCT01874054) or gemcitabine (NCT01780662). In particular, LaCasce et al20 reported the preliminary data on a phase 1/2 single-arm study to evaluate the safety and efficacy of BV in combination with bendamustine for patients with HL in the first salvage setting. Among 13 available patients, 10 (77%) experienced a CR, and 2 (15%) experienced a PR with an ORR of 92% after 2 cycles of bendamustine plus BV.

Therapy in Newly Diagnosed Patients. BV in newly diagnosed HL has been proposed under the rationale that the rate of therapy-related acute and long-term toxicity with BV might be lower than with conventional chemotherapy, and that the cure rate achieved with front-line BV containing chemotherapy regimens may be improved. A phase 1/2 study showed an excellent response rate of 95% for the combination of BV and ABVD (Adriamycin, bleomycin, vinblastine, dacarbazine) in newly diagnosed HL patients.21 However, the combination of BV and ABVD was associated with an unacceptably high rate of serious pulmonary events. Therefore, the protocol was modified, and patients subsequently received BV combined with AVD until accrual was completed.21 Response rates appeared not to be compromised by the omission of bleomycin, and no more pulmonary events occurred after switching from ABVD to AVD. Of note, BV is provided at a dose of 1.2 mg/kg every 2 weeks when combined with AVD. A phase 3 trial (NCT01712490) randomly compared classical ABVD with a combination of BV and AVD in patients with newly diagnosed advanced HL. In a different approach, the German Hodgkin Lymphoma Study group is conducting a clinical trial incorporating BV with modified escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine [Matulane], prednisone) regimen (NCT01569202). At the same time, Yasenchak et al22 reported the interim results of a phase 2 study of single-agent BV for front-line treatment of HL in patients aged 60 years and older; among 19 efficacy-evaluable patients, the ORR was 89%, with 12 patients experiencing CR. In a preliminary report, Federico et al23 reported that 2 cycles of BV induced a complete metabolic response in 10 (83%) of 12 enrolled patients with previously untreated, limited-stage HL.

Recommendations.

- According to the FDA and the European Medicines Agency (EMA), BV is indicated for the treatment of patients with HL after failure of ASCT or after failure of at least 2 prior multiagent chemotherapy regimens in patients who are not ASCT candidates.
- The EP agreed that there is now evidence for recommending BV also in HL patients with disease refractory to salvage chemotherapy who are ASCT candidates and as a consolidation strategy after ASCT.
- The use of BV in HL after relapse from allo–stem-cell transplantation (SCT) or as first-line therapy is at present only experimental.

Practice Indications of BV in Systemic Anaplastic Large-Cell Lymphoma

After initial chemotherapy, sALCL has an expected recurrence rate of 40% to 60%, and only 25% to 30% of patients experience a second CR with combination chemotherapy. The typical duration of the second remission is less than 1 year.24

In the initial phase 1 trial with BV, only 2 out of 45 patients had sALCL (ALK positive), and both experienced CR.9 The efficacy of BV in relapsed or refractory sALCL was evaluated in an open-label, single-arm, phase 2 trial involving 58 patients (72% ALK negative).25 The ORR was 86% and CR 57%, with a median response duration of 13.0 months. Median PFS was 14.6 months, and median overall survival was not reached at the time of publication. ORR and CR rate, median PFS, and duration of response were not different according to ALK status. In addition, the likelihood of
experiencing CR was not influenced by disease status (relapsed vs. primary refractory disease), prior ASCT, or bone marrow involvement.

After these positive results, BV was approved in August 2011 by the FDA for the treatment of sALCL after failure of at least 1 chemotherapy regimen. Subsequently, the EMA licensed BV for this indication.

New relevant questions on the use of BV outside the approved indications include its use earlier in the disease course by combining with first-line regimens like CHOP (cyclophosphamide, doxorubicin hydrochloride [hydroxydaunomycin], vincristine sulfate [Oncovin], prednisone) or CHP (CHOP without vincristine). In a recent phase 1 trial, patients with ALK-positive sALCL and International Prognostic Index ≥ 2 received 2 different schedules of BV and CHOP chemotherapy. In arm 1, 13 patients (3 ALK-negative) received 2 cycles of 3 weekly 1.8 mg/kg BV, then CHOP (CR 38% with BV initially; after CHOP, CR 62%). After sequential treatment, 12 of 13 patients remained on treatment and received single-agent BV. After a median observation of 23 months, 1-year PFS was 77%. In the other group, 26 (19 sALCL) patients received combination BV plus CHP. Twenty-three of 26 patients completed 6 cycles of BV plus CHP, and 21 received subsequent single-agent BV. Response assessment was performed at the end of BV + CHP treatment (6 cycles). The ORR was 100% and CR 88%. The 1-year PFS rate was 71%.

A randomized phase 3 trial is currently underway to compare BV plus CHP versus standard-of-care CHOP in CD30-positive mature PTCL (NCT01777152).

Recommendations.
- According to the FDA and EMA, BV is indicated for the treatment of patients with sALCL with disease refractory to previous therapy or patients who experienced relapse after first-line therapy, regardless of ALK status and number of prior treatments. The EP agreed on recommending these as stringent indications of use.
- Other uses of BV, like that of BV in combination with first-line regimens, are experimental.

Pretreatment Evaluation of BV Candidates

The EP discussed the most appropriate way to evaluate the disease burden before BV treatment in order to better assess the response to treatment. According to the revised response criteria for lymphomas, 18F-fludeoxyglucose–positron emission tomography (FDG-PET) is strongly recommended before treatment for patients with FDG-avid lymphomas such as HL to better delineate the extent of the disease.11

In clinical trials with BV provided as a single agent to treat HL or sALCL, baseline evaluations included documentation of disease-related signs and symptoms, physical examination, bone marrow biopsy, and radiographic studies, including computed tomography (CT) of the neck, chest, abdomen, and pelvis, and PET scan. In studies reporting patients treated with BV either in a NPP or in the context of safety studies associated with the registration program of the drug, different schedules of pretreatment evaluation were used.

In the German study, CT but not PET was mandatory at initial staging.11 In the Italian study, all patients underwent baseline assessment including PET/CT studies.13

The results of an observational study with a small cohort of patients indicate that FDG-PET/CT is able to monitor metabolic treatment response in patients treated with BV and helps to identify patients with improved clinical outcome early during treatment. This evidence prompted the EP to suggest FDG-PET scan in all patients at initial staging before therapy as a tool to better test response.28

Recommendation.
- Patients who are candidates for BV should receive an accurate staging of disease that includes PET and CT scan before starting treatment. Bone marrow biopsy should be performed only when clinically indicated.

Monitoring the Response to BV

The Biological License Application for BV was the first application submitted to the FDA using the 2007 revised response criteria for lymphomas, which may include FDG-PET scans in the response assessment. However, FDA or EMA approval did not produce specific indications on the best schedule to assess response.

The intervals between periodic assessments of response and surveillance varied among BV clinical trials. In the initial phase 1 study, response was assessed after every 2 cycles (every 6 weeks).9 In the phase 2 study in sALCL, response was assessed after every 2 cycles (every 8 weeks).24 In the pivotal study of BV in relapsed or refractory HL, tumor response assessments were performed by CT scans at cycles 2, 4, 7, 10, 13, and 16 and by PET scans at cycles 4 and 7.10 The study reported also a median time to objective response of 5.7 weeks (approximate time of the first postbaseline CT scan); the median time to CR was 12 weeks (approximate time of the first postbaseline PET scan). The majority of responses occurred early during the treatment, but 1 CR was documented after approximately 1 year of therapy.

In nontrial reports, the monitoring strategy also varied. In the German study, staging and restaging CT was mandatory; however, the time point of the restaging CT scans was not defined.11 A total of 34 patients also underwent PET to determine the metabolic response. In the Italian study, response was assessed by PET/CT scan after cycles 3 and 8 and at treatment discontinuation, as reported in the pivotal study.13

The EP claimed that an early PET evaluation is advisable; furthermore, as with other treatments, further evaluation of response is advisable before SCT, if planned.

Recommendations.
- Patients treated with BV for HL should be clinically monitored at each cycle of therapy. A PET scan should be performed after cycle 4.
- A final response assessment at the end of therapy in HL should include a complete evaluation of the patient, including PET and CT scans.
- Patients treated with BV for sALCL should be monitored for response after 4 courses of therapy with CT scan.
- Further evaluation of response should be done before SCT, if planned, or after 8 cycles of therapy.
• A final response assessment at the end of therapy in sALCL should include a complete evaluation of the patient and a CT scan.

Management of Patients Treated With BV

Treatment Duration. The overall management of patients treated with BV varied among clinical trials. In the initial phase 1 study, patients with CR, PR, or stable disease with protocol-defined clinical benefit (improved performance status, decreased analgesic consumption, or decreased disease volume) could continue therapy. Study treatment was discontinued at confirmation of disease progression. Data of the pivotal phase 2 trial in HL indicate that it might take more than 4 courses to achieve the best response to BV, suggesting a decision about high-dose chemotherapy and ASCT after the fourth course of BV.10

In nontrial reports, the treatment strategy varied. In the German study, treatment was continued until disease progression.11 The major result of the Italian study indicates that the best responses, and thus further therapy decisions, should occur after 3 or 4 cycles of therapy.13

Retreatment With BV. Appropriateness of retreatment with BV in HL and sALCL was investigated in a prospective study of 29 patients (21 HL, 8 sALCL) who had experienced relapse after experiencing CR or PR with BV. Among the 20 HL patients who were evaluable for efficacy, 12 (60%) experienced a response (6 CR, 6 PR). The median response duration among patients responding to BV retreatment was 9.4 months. Side effects were similar to those seen after initial treatment. However, the rate of peripheral neuropathy appeared to be higher than after initial BV treatment, so extended BV exposure should be closely monitored for this adverse effect.

Bartlett et al29 reported that retreatment with BV monotherapy was associated with 68% relative risk (39% CR) in patients with relapsed HL and sALCL.

Allogeneic Transplantation After BV. The role of allogeneic SCT (allo-SCT) as a salvage regimen after BV and the impact of BV on allo-SCT were retrospectively examined in 3 studies.18,30,31 Although the study was of a small series of patients, all 3 studies reported a very favorable outcome in relapsed or refractory HL in patients who received allo-SCT after response to BV. Additionally, BV before reduced-intensity allo-SCT does not appear to adversely affect engraftment, graft versus host disease, or survival, and may provide sufficient disease control to enable reduced-intensity allo-SCT.30

Peripheral Sensory Neuropathy. BV was designed to deliver the cytotoxic agent specifically to tumor cells, thereby resulting in an improved safety profile. The most common treatment-related emergent adverse event is peripheral sensory neuropathy, occurring after prolonged exposure to the drug. In the AETHERA study, the median time to onset of peripheral neuropathy events was 13.7 weeks.19 Patients can experience numbness and tingling of the fingers and toes. Resolution of the symptoms after dose modification or therapy discontinuation occurred in 85% of the cases.

Recommendations.

• In the approved indications of BV treatment for HL and sALCL, treatment evaluation must be performed after 4 courses, and the subsequent treatment should be determined according to the response.

• In patients with HL who experience a CR, either an early consolidation program including allo-SCT or BV therapy continued up to 16 cycles are the approved indications of use. The EP did not reach a consensus on which of the 2 strategies was more appropriate. More clinical trials are needed.

• In patients with HL who experience a partial response, early allo-SCT should be considered. Patients not eligible for a transplant should be treated with BV up to a maximum of 16 cycles.

• In patients with HL and a stable disease, the decision to continue BV should rely on a patient-centered balance between clinical benefits and risks.

• In patients with HL and progressive disease, BV therapy should be discontinued.

• In patients with sALCL who experience a CR after a strategy not including ASCT, ASCT is the preferred therapy. In patients who experience a CR after a strategy including ASCT, either an early consolidation program including allo-SCT or BV therapy up to 16 cycles is an approved indication of use. The EP agreed that both of these strategies are clinically appropriate. More clinical trials are needed.

• In patients with sALCL who experience a partial response, an early consolidation program including SCT is the recommended strategy. ASCT or allo-SCT in patients who had a previous strategy including ASCT were judged as the most appropriate candidates for this therapy. Patients not eligible for a transplant should be treated with BV up to a maximum of 16 cycles.

• Patients with sALCL and stable or progressive disease should be shifted to an alternative treatment.

• Patients with either HL or sALCL who experience relapse after a complete or partial remission with initial BV therapy may be retreated with BV.

• Patients should be monitored for symptoms of neuropathy, such as paresthesia, neuropathic pain, and weakness. For grade 2 or higher or worsening neuropathy, dosing should be delayed until neuropathy improves to grade 1 or baseline. Then BV should be considered to be restarted at 1.2 mg/kg. For grade 4 peripheral neuropathy, BV should be discontinued.

Role of BV in Other CD30-Positive Lymphomas

Preliminary results have shown the efficacy of BV in other subtypes of non-HLs that have various levels of CD30-positive cells, including diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma,32 PTCL not otherwise specified, angioimmunoblastic T-cell lymphoma,33 and cutaneous T-cell lymphoma.34,35

Activity of BV has been demonstrated in individual cases with enteropathy-associated T-cell lymphoma,36 plasmablastic lymphoma arising from a background of chronic lymphocytic leukemia,37 posttransplantation lymphoproliferative disorders,38 and effusion lymphomas.39
Brentuximab Vedotin in CD30-Positive Lymphomas

Recommendations.

- There are no data to recommend the use of BV outside clinical trials for patients with PTCLs (but anaplastic large-cell lymphoma), cutaneous T-cell lymphoma, primary mediastinal large B-cell lymphoma, and diffuse large B-cell lymphoma.
- The documented major activity of this pleiotropic drug on CD30/CD30L signaling should encourage the enrollment of patients with incurable lymphomas into clinical trials using BV.

Discussion

Experts in lymphomas judged whether the body of evidence was sufficient to provide recommendations regarding the use of BV in an on-label or off-label use, and how to optimize the approved use of the drug. The efficacy and safety of BV were well established in relapsed or refractory HL and sALCL. Recent evidence showed that the drug may be safely and effectively used before ASCT in HL, and as retreatment in the approved indications of use. Thus, the EP extended the recommendations of use to HL patients whose disease had failed to respond to at least 2 prior chemotherapy regimens regardless of their eligibility for ASCT and to facilitate consolidation allo-SCT after BV treatment.

Recently updated National Comprehensive Cancer Network (NCCN) guidelines were concordant in indicating that HL patients with disease refractory to second-line chemotherapy should not proceed to high-dose therapy and ASCT, and those with progressive or relapsed disease whose disease is not chemosensitive after 2 chemotherapy regimens should be provided a trial of BV before ASCT, even though they may be candidates for a transplant. In line with approved indications of use and our recommendations, NCCN guidelines recommended that sALCL patients who are candidates for transplant would be treated with second-line regimens, and BV was included among the suggested treatments.

Acknowledgments

Funding of the project was provided by SIE, SIES, and GITMO with an at-arm’s-length contribution from Takeda Italy provided to SIE. The SIE administered all aspects of the meetings. The funding sources had no role in identifying statements, abstracting data, synthesizing results, or preparing the manuscript, or in the decision to submit the manuscript for publication.

Disclosure

The authors have stated that they have no conflicts of interest.

References


