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Brentuximab Vedotin Compared with Other Therapies in Relapsed/Refractory Hodgkin Lymphoma Post ASCT: Median Overall Survival Meta-Analysis

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Abstract

Objective: This meta-analysis compared the median overall survival (mOS) of brentuximab vedotin reported in the pivotal phase 2 study with published results of other therapies for the treatment of relapsed/refractory (R/R) Hodgkin lymphoma (HL) post-autologous stem cell transplant (ASCT).

Research design and methods: A systematic literature review identified studies that reported survival outcomes following conventional/experimental therapies in R/R HL patients, with ≥50% having failed ≥1 ASCT. Kaplan–Meier curves were used to reconstruct individual

patient level survival data. Patients were grouped by treatment type and reconstructed data were used to estimate the mOS. Censored median regression modelling was used to compare mOS in each group with the mOS in the pivotal brentuximab vedotin trial. All patients in the pivotal trial had undergone ASCT, therefore a sensitivity analysis was conducted among studies with a 100% post-ASCT patient population.

Results: The mOS reported for brentuximab vedotin was 40.5 (95% CI 30.8-NA) compared with 26.4 months (95% CI 23.5-28.5) across all 40 studies identified (n=2518 excluding the brentuximab vedotin trial) (p<0.0001). The difference in mOS between brentuximab vedotin and chemotherapy, allogeneic stem cell transplant (allo-SCT), and other therapies, was 17.7 (95% CI 10.6-24.7; p<0.0001), 12.5 (95% CI 8.2-16.9; p<0.0001), and 15.2 months (95% CI 4.9-25.5; p=0.0037), respectively. For the 11 studies reporting a 100% prior-ASCT rate (n=662 excluding the brentuximab vedotin trial), the mOS was 28.1 months (95% CI 23.9-34.5), and the difference in mOS between brentuximab vedotin, chemotherapy, allo-SCT, and other therapies was 19.0 (95% CI 12.9-25.1; p<0.0001), 9.4 (p>0.05), and 6.8 months (95% CI 1.2-12.5; p=0.0018), respectively.

Conclusions: While some selection bias may occur when comparing trials with heterogeneous eligibility criteria, in the absence of randomized controlled trial data these results suggest brentuximab vedotin improves long-term survival and is associated with longer mOS in R/R HL post-ASCT compared with other therapies.

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Brentuximab Vedotin Compared with Other Therapies in Relapsed/Refractory Hodgkin Lymphoma Post ASCT: Median Overall Survival Meta-Analysis

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Key words: Meta-analysis, Hodgkin lymphoma, Antigens, CD30, Hematopoietic Stem Cell Transplantation, Overall survival, Brentuximab vedotin.

[Short title: Brentuximab vedotin in relapsed/refractory Hodgkin lymphoma

Abstract:

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Research design and methods: A systematic literature review identified studies that reported survival outcomes following conventional/experimental therapies in R/R HL patients, with \geq 50% having failed \geq 1 ASCT. Kaplan–Meier curves were used to reconstruct individual patient level survival data. Patients were grouped by treatment type and reconstructed data were used to estimate the mOS. Censored median regression modelling was used to compare mOS in each group with the mOS in the pivotal brentuximab vedotin trial. All patients in the pivotal trial had undergone ASCT, therefore a sensitivity analysis was conducted among studies with a 100% post-ASCT patient population.

Results: The mOS reported for brentuximab vedotin was 40.5 (95% CI 30.8-NA) compared with 26.4 months (95% CI 23.5-28.5) across all 40 studies identified (n=2518 excluding the brentuximab vedotin trial) (p<0.0001). The difference in mOS between brentuximab vedotin and chemotherapy, allogeneic stem cell transplant (allo-SCT), and other therapies, was 17.7 (95% CI 10.6-24.7; p<0.0001), 12.5 (95% CI 8.2-16.9; p<0.0001), and 15.2 months (95% CI 4.9-25.5; p=0.0037),

respectively. For the 11 studies reporting a 100% prior-ASCT rate (n=662 excluding the brentuximab vedotin trial), the mOS was 28.1 months (95% CI 23.9-34.5), and the difference in mOS between brentuximab vedotin, chemotherapy, allo-SCT, and other therapies was 19.0 (95% CI 12.9-25.1; p<0.0001), 9.4 (p>0.05), and 6.8 months (95% CI 12.-12.5; p=0.0018), respectively.

Conclusions: While some selection bias may occur when comparing trials with heterogeneous eligibility criteria, in the absence of randomized controlled trial data these results suggest brentuximab vedotin improves long-term survival and is associated with longer mOS in R/R HL post-ASCT compared with other therapies.



Introduction

Hodgkin lymphoma (HL) is a rare clonal lymphoid malignancy, with an annual incidence rate of 2.90 and 2.49 per 100,000 in the US and Europe, respectively^{1, 2}. It is estimated that in 2014 there will be 9,190 new HL diagnoses and 1,180 deaths in the US alone³. Currently, more than 80% of all newly diagnosed HL patients, aged ≤ 60 years, are likely to be cured following front-line therapy consisting of multi-agent chemotherapy and radiotherapy^{4, 5}. However, depending on the initial stage of the disease at diagnosis as well as the various prognostic factors, up to 30% of patients who achieve remission, relapse or are refractory to frontline therapy^{6, 7}. For patients with relapsed/refractory (R/R) HL, standard treatment involves second-line, salvage combination chemotherapy followed by highdose chemotherapy and autologous stem cell transplant (HDT-ASCT)^{8, 9}. Unfortunately, approximately 50% of HL patients relapse after ASCT^{10, 11} and their prognosis is generally poor with a median survival of 25 months¹². Treatment options for R/R HL patients post-ASCT are limited and include additional chemotherapy. The management of this subset of patients remains a significant challenge.

Brentuximab vedotin is an antibody-drug conjugate that targets CD30^{13, 14}, a cell-surface antigen expressed on the malignant Hodgkin's Reed-Sternberg cells of classical HL¹⁵. It consists of a CD30-targeted monoclonal antibody (cAC10) covalently linked to the microtubule-disrupting agent monomethyl auristatin E (MMAE) by a protease-cleavable linker^{13, 14, 16, 17}. It received accelerated approval from the US Food and Drug Administration in 2011 for the treatment of HL patients that have relapsed after ASCT or after at least two prior multi-agent chemotherapy regimens with ineligibility for ASCT¹⁸. Subsequently, brentuximab vedotin received conditional approval from the European Commission in 2012 for the treatment of CD30-positive R/R HL patients after ASCT or after failure of at least two prior multi-agent chemotherapy regimens when ASCT or multi-agent chemotherapy is not a treatment option¹⁹.

The efficacy and safety of brentuximab vedotin in R/R HL post-ASCT was demonstrated in a single-arm, multicentre, pivotal phase 2 clinical trial (SG035-0003; NCT00848926)²⁰. A total of 102 patients with R/R HL following ASCT were treated with brentuximab vedotin 1.8 mg/kg by intravenous infusion every 21 days for a maximum of 16 cycles. The objective response rate was 75%, with complete remission (CR) in 33% of patients^{20, 21}. Recent long term follow-up data from the pivotal phase 2 trial, with a median observation time of 32.7 months, reported a median overall survival (mOS) of 40.5 months²².

The US and European approval of brentuximab vedotin for the treatment of R/R HL was based on the results of the pivotal phase 2 study. In the absence of head-to-head, randomized, controlled, phase 3 trials, no comparative efficacy data for brentuximab vedotin and existing therapies in the R/R setting are available. A recent meta-analysis compared the antitumor activity of brentuximab vedotin in terms of CR rate as reported in the phase 2 study, with existing drug therapies or experimental agents, for the treatment of R/R HL post-ASCT. Brentuximab vedotin was associated with a significantly higher CR rate compared with other therapies (33.3% vs. 11.1%, p<0.0001)²³. Now that long-term survival data are available for patients treated with brentuximab vedotin in the pivotal phase 2 study, we conducted a systematic literature review to identify studies which reported survival outcomes for other therapies among adult R/R HL patients post-ASCT. We then performed a meta-analysis to compare the mOS of brentuximab vedotin as reported in the pivotal study to that of other therapies reported in the literature for the treatment of R/R HL post-ASCT patients.

Patients and methods

Systematic literature review

Per pre-specified criteria, a systematic literature review was undertaken to identify studies that reported survival outcomes following conventional and experimental therapies in R/R HL patients

post-ASCT. Indexed search terms and free text terms were used to identify 'relapsed', 'refractory', 'HL', and 'ASCT' in studies published between February 2013 and January 2014 in six electronic databases: MEDLINE, MEDLINE In-Process and other non-indexed citations, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP). Recent conference proceedings (2011 to 2013) from American Society for Clinical Oncology (ASCO), American Society of Hematology (ASH), European Society of Medical Oncology (ESMO), and European Hemtology Association (EHA) were also included. There were no restrictions regarding study design or type of treatment in the initial search, and Englishlanguage studies involving human subjects were selected for review. A comprehensive summary of the search strategies with detailed search terms is provided in the supplementary appendix. Relevant studies published from January 1993 to January 2013, identified from a prior systematic literature review that was conducted using the same search strategy as the current study, were included in the final analysis.

Studies identified from both the current and prior systematic literature review were selected for relevance for the subsequent meta-analysis, by a two level screening process, according to predetermined inclusion and exclusion criteria. The results are reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement²⁴. Studies were screened by title and/or abstract at the first level followed by full text screening at the second level. Clinical trials from the ICTRP were screened by title, by trial description, and by full text of any linked publication. The inclusion criteria required that the study population include \geq 20 R/R HL patients, of whom \geq 80% were \geq 12 years of age and \geq 50% had failed at least one ASCT. Included studies were to report survival outcomes, specifically Kaplan–Meier (KM) curves, mOS, and survival rates. Kin studies deemed non-primary publications for a study and not reporting relevant outcomes were excluded, as were studies reporting survival time from time points other than the start of the treatment under evaluation and studies reporting actuarial survival rate. Certain publication types were excluded including reviews, meta-analyses, comments, recommendations/guidelines, study protocols, and case reports.

Data collection

Two reviewers independently extracted data from each eligible study which were collected in

a pre-specified extraction table. Where available, extracted data included bibliographic information, study description and design (type of study, time frame, location of study, condition, number of HL patients, and number of study arms), patient baseline demographics and disease characteristics, study treatment(s), and clinical outcomes (KM curves and/or mOS). Any discrepancies were discussed or a third reviewer was consulted to reach a consensus.

Statistical analysis

Studies that included KM curves of OS, estimated from the start of treatment under evaluation, were used to reconstruct pseudo-individual patient level survival data survival or censoring times at the pseudo-individual patient level. Engauge digitization software (v4.1) was used to extract time points and survival probabilities from the published KM curves. Pseudo-individual patient level data were reconstructed from the digitized curves using the published algorithm recommended by the National Institute for Health and Care Excellence (NICE), UK^{25, 26}. Patients were grouped according to the type of post-ASCT treatment they received (brentuximab vedotin, chemotherapies, allo-SCT, or other therapies), and the reconstructed pooled datasets were used to plot a single KM curve and estimate the mOS and 95% confidence interval (CI) for each treatment group identified. Reconstructed survival data was validated by comparing the estimated mOS with those reported in published studies (or derived from published KM curves using pixel analysis). In addition, reproduced KM curves from four randomly selected studies (one from each treatment group) were overlaid on top of the original published curves and the level of agreement was visually assessed.

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A censored quantile regression model²⁷ was used to estimate the difference in mOS obtained from the long-term follow-up results for the pivotal phase 2 brentuximab vedotin trial with the other treatment groups, and the p-value of the difference. A log-rank test was also performed to test for overall differences between the KM curves of brentuximab vedotin versus alternative treatment groups as a whole. All analyses were carried out using the statistical software R (v2.15.2). Two sensitivity analyses were carried out; one including only those studies reporting a 100% prior-ASCT patient population to assess the impact of prior-ASCT on the estimated mOS for each treatment group, and one using a relaxed classification for chemotherapy including all studies reporting either sole chemotherapy regimens or chemotherapy in combination with other treatments to better reflect the diverse treatment regimens that patients may receive in clinical practice.

Results

Selection of studies

The systematic literature search process is shown in Figure 1. Our initial search identified a total of 787 potentially relevant records. An additional 121 records published between January 1993 and February 2013 were obtained from the prior systematic literature review. Forty-eight studies met the required criteria after full-text screening. The most frequent reasons for exclusion were studies without relevant populations (*n*=48) or outcomes (*n*=20). Forty one of these 48 studies, including the brentuximab vedotin pivotal trial, with a total of 2,619 evaluable R/R HL patients, reported KM curves of OS among R/R HL post-ASCT patients and were included in the meta-analysis^{22, 28-67}. The study design and key patient characteristics for all 41 studies included in the meta-analysis are described in Table 1. They consisted of 1 phase 1/2, 11 phase 2, 8 prospective cohort, and 21 retrospective studies. The most commonly observed treatment types were allo-SCT and chemotherapy with 21 and 8 studies reporting survival outcomes, respectively. Chemotherapy under evaluation

included single sequential or multi-agent treatments, and the agent used varied, including gemcitabine (n=3), bendamustine (n=3), vinorelbine (n=4), and pegylated liposomal doxorubicin (n=2). The remaining 11 studies reported outcomes for other therapies including radiation therapy, immunotherapies such as donor leukocyte infusions, and mixed treatments such as radiation therapy in combination with salvage chemotherapy.

The studies varied in size, with the number of HL patients in each study ranging from 21 to 285. The median age of all patients ranged from 25 to 51 years, the median number of prior regimens ranged from $\leq 2-5$, and the number of patients with previous ASCT ranged from 52 to 100%. In the pivotal study of brentuximab vedotin, the median age was 31 years (range: 15-77), the median number of prior chemotherapy regimens was 3.5 (range: 1-13), and all patients had undergone ASCT²². Twelve studies, including the brentuximab vedotin phase 2 trial, with a total of 763 evaluable R/R HL patients, reported a 100% prior-ASCT rate and were included in the sensitivity analysis. Of these 11 remaining studies, 4 reported outcomes for chemotherapy, 3 for allo-SCT, and 4 for other therapies.

Analysis of mOS

The estimated mOS in R/R HL post-ASCT patients across the 40 pooled studies of current treatment was 26.4 months (95% CI 23.5-28.5). This was significantly lower than the reported mOS of 40.5 months (95% CI 30.8-NA; p < 0.0001) for patients receiving brentuximab vedotin in the pivotal phase 2 trial. The results of the meta-analysis are presented in Figure 2. The estimated mOS for chemotherapy, allo-SCT, and other treatment regimens was 23.0 months (95% CI 21.0-28.1), 27.9 months (95% CI 23.9-30.2), and 23.9 months (95% CI 21.0-28.0), respectively. Brentuximab vedotintreated patients experienced significantly longer mOS compared with patients on chemotherapies, allo-SCT, and other treatment regimens as demonstrated by differences in mOS of 17.7 months (95%

CI 10.6-24.7; *p*<0.0001) (Figure 2a), 12.5 months (95% CI 8.2-16.9; *p*<0.0001) (Figure 2b), and 15.2 months (95% CI 4.9-25.5; *p*=0.0037) (Figure 2c), respectively.

The sensitivity meta-analysis, which included only those studies that reported a 100% prior-ASCT rate, showed a significant difference between the reported mOS of 40.5 months in the brentuximab vedotin trial and the estimated mOS across the 11 pooled studies of 28.1 months (95% CI 23.9-34.5; p<0.0001). The results of this sensitivity meta-analysis are presented in Figure 3. The estimated mOS for chemotherapy, allo-SCT, and other treatment regimens in the sensitivity metaanalysis was 21.1 months (95% CI 17.0-28.1), 31.1 months (95% CI 23.9-62.1), and 34.1 months (95% CI 29.5-41.5), respectively. Brentuximab vedotin-treated patients experienced significantly longer mOS compared with patients on chemotherapies, and other treatment regimens as demonstrated by differences in mOS of 19.0 months (95% CI 12.9-25.1; p<0.0001), and 6.8 months (95% CI 1.2-12.5; p=0.0018), respectively. The median difference in mOS estimated from the censored quantile regression method between patients receiving brentuximab vedotin and allo-SCT was not reported as the assumption of monotonicity for quantile difference was not met; however, the raw numeric difference of 9.4 months was not statistically significant (p>0.05).

The sensitivity meta-analysis, which grouped studies using a relaxed classification for chemotherapy, further demonstrated that brentuximab vedotin-treated patients experienced a significantly longer mOS compared with patients on chemotherapies. The estimated mOS for the broad chemotherapies group was 22.2 months (95% CI 21.0-27.5). The difference in mOS between brentuximab vedotin and broad chemotherapies was 17.3 months (95% CI 9.9-24.7; p<0.0001) (Figure 4).

Discussion

This meta-analysis is the first study to compare mOS between brentuximab vedotin and other therapies for the treatment of adult patients with R/R HL post-ASCT. In the absence of randomized controlled trial data, this study allows for an indirect comparison of survival outcome between brentuximab vedotin and current therapies used in the R/R setting. Brentuximab vedotin was associated with a significantly longer mOS compared with that of other therapies reported in the literature (40.5 months vs. 26.4 months, p<0.0001). The difference in mOS between brentuximab vedotin and chemotherapy, allo-SCT, and other therapies was 17.7 months (p<0.0001), 12.5 months (p<0.0001), and 15.2 months (p=0.0037), respectively. Our results suggest brentuximab vedotin improves long-term survival in adult R/R HL patients.

The results of this meta-analysis are consistent with those reported from previous metaanalyses. Using a similar methodological approach, Bonthapally et al. conducted a meta-analysis to evaluate the antitumor activity of brentuximab vedotin as reported in the pivotal phase 2 study versus the activity of other drug therapies and experimental agents as reported in 17 evaluable studies identified from the literature, in patients with R/R HL post-ASCT. CR rate was selected as the most appropriate endpoint for the study due to the lack of long-term survival data for patients treated with brentuximab vedotin. Brentuximab vedotin was associated with a significantly higher CR rate compared with other therapies in the treatment of R/R HL post-ASCT patients (33.3% vs. 11.1%, p < 0.0001²³. Karuturi et al. compared OS from the pivotal brentuximab vedotin study with 756 R/R HL historical control post-ASCT patients from 6 international centres, prior to the approval and widespread availability of brentuximab vedotin. Brentuximab vedotin was associated with prolonged mOS, measured from the point of ASCT, when compared with historical control patients (91.49 months vs. 27.99 months, p < 0.0001). Improvement in OS was irrespective of time to relapse post-ASCT, age, or sex⁶⁸. These findings further support the results of our study suggesting that brentuximab vedotin's antitumor activity exceeds that of other therapies currently used in the treatment of R/R HL post-ASCT. Our study provides a comprehensive review of the literature to date, comparing brentuximab vedotin's efficacy, in terms of mOS, with other therapies used to treat R/R HL post-ASCT using long-term survival data over a 24-month period.

In the absence of well controlled head-to-head comparisons, meta-analyses such as this provide valuable insights; however, results should obviously be interpreted with caution. We acknowledge the potential for patient selection bias that may occur when comparing trials with heterogeneous eligibility criteria. The systemic literature review identified 41 studies that met all eligibility criteria and presented KM curves of OS for inclusion in the meta-analysis. There was substantial heterogeneity in the mOS reported within each treatment group. In the studies for chemotherapy, allo-SCT, and other therapies, mOS ranged from 12^{58} to $42^{35, 39}$ months, 6.7^{62} to 55^{51} months, and 14.8³⁶ to 40.8⁴⁶ months, respectively. Nine studies had relatively short follow-up time so that mOS were not reached by the end of the study period^{29, 30, 45, 48, 50, 53, 54, 66, 67}. With the inclusion of these immature data, the censored quantile regression model was likely to over-estimate mOS for the treatment group; however, the final impact of these immature data on the meta-analysis is unclear. Survival data for brentuximab vedotin were obtained from the pivotal phase 2 trial, where all 102 patients had undergone ASCT prior to receiving brentuximab vedotin; however, only 11 out of the 40 pooled studies of other treatments reported a 100% prior-ASCT rate. Therefore, we conducted a sensitivity analysis among only those studies reporting a 100% post-ASCT population, to examine the effect of ASCT status on the primary result. Our findings confirmed the robustness of the brentuximab vedotin mOS result compared with that of other therapies reported in the literature (40.5 months vs. 28.1 months, p<0.0001). The median difference in mOS between brentuximab vedotin and chemotherapy, and other therapies for the 100% prior-ASCT patient population was 19.0 months (p < 0.0001), and 6.8 months (p = 0.0018), respectively, further suggesting brentuximab vedotin improves long-term survival compared to other treatment types. The raw numeric difference of 9.4 months (p>0.05) between 100% prior-ASCT patient receiving brentuximab vedotin and allo-SCT was not statistically significant; however, this may be due to the low number of allo-SCT studies reporting survival outcomes for a 100% prior-ASCT patient population.

Due to the lack of individual patient baseline characteristics reported in the studies, they could not be adjusted for effect modifiers in the censored quantile regression model to account for differences in observed baseline characteristics. This could have led to biased estimates. Furthermore, as the studies included in the meta-analysis were either single-arm or lacked common comparator arms, it was not possible to make adjustments to account for differences in unobserved baseline characteristics. Finally, it is important to note that this meta-analysis compared three alternative treatment groups to brentuximab vedotin: chemotherapies, allo-SCT, and other therapies. The chemotherapy group included studies where patients only received chemotherapy agents. Mixed treatments, such as chemotherapies in combination with salvage radiation therapy were categorized in the other therapies group. In clinical practice, patients do not fall exclusively into one treatment category, but receive multiple salvage treatment regimens depending on their age, performance status, disease type and stage, and time to relapse⁶⁹. We therefore conducted a sensitivity analysis using a relaxed classification for chemotherapy to better reflect clinical practice. The estimated mOS for the broad chemotherapies group was 22.2 months (95% CI 21.0-27.5), which was significantly lower compared to patients receiving brentuximab vedotin as demonstrated by a difference in mOS of 17.3 months (95% CI 9.9-24.7; p<0.0001). Analysis of safety data was beyond the scope of this metaanalysis.

Future analyses which can prospectively compare brentuximab vedotin to alternative therapies using a randomized design are needed to verify the findings from the current study. Two randomized, multicentre phase 3 brentuximab vedotin studies are ongoing; however, these are not in the R/R HL post-ASCT population. AETHERA (NCT01100502) is a double-blind, placebo-controlled study investigating brentuximab vedotin and best supportive care (BSC) versus placebo and BSC in the treatment of HL patients at risk of progression following ASCT. Efficacy data were recently published. As of August 2013, all patients have completed or discontinued study treatment⁷⁰. ECHELON-1 (NCT01712490) is an open-label study, investigating the safety and efficacy of front-line brentuximab vedotin plus doxorubicin, vinblastine, and dacarbazine (AHAVD) versus doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) in patients with advanced-stage classical HL. As of June 23, 2014, 444 patients have been randomized at 195 sites; data is expected to be published in the near future.

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Conclusion

Results of this meta-analysis suggest that brentuximab vedotin is associated with a longer mOS compared with other therapies among patients with R/R HL post-ASCT. In the absence of randomized clinical trials, our findings suggest brentuximab vedotin improves long-term survival and provides meaningful clinical benefit in adult R/R HL patients.

Transparency

Declaration of funding:

The analysis was funded by Millennium Pharmaceuticals Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

Declaration of financial/other relationships:

VB, AC, DH are employed by Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited; VB owns stocks in Takeda Pharmaceutical Company Limited; AG is employed by Millennium Pharmaceuticals, Inc.; HY, RA, RDT, SC, EW are employees of Analysis Group Inc., which has received a consultancy fee from Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited. CMRO Peer Reviewers on this manuscript have received an honorarium from CMRO for their review work, but have no other relevant financial relationships to disclose.

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Figure 2. Comparison of mOS for brentuximab vedotin versus (A) chemotherapy, (B) allo-SCT, and (C) other therapies.

















chemotherapy, allo-SCT, and other therapies in patients with a 100% prior-ASCT rate



chemotherapy using a relaxed classification for chemotherapy



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Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
			HL patients	years	prior ASCT, <i>n</i> (%)	(months)	from KM curve [†]), month
Alvarez et al ²⁸	Prospective cohort	Allo-SCT with RIC	40	35	29 (73)	8.5	20^{\dagger}
Anastasia et al ²⁹	Prospective cohort	Bendamustine	69/73	34	73 (100) [‡]	13	Not reached
Anderlini et	Retrospective	Allo-SCT with RIC	40	31	30 (75)	12 (all patients) 13 (survivors)	Not reached
Anderlini et al ³¹	Prospective cohort	Allo-SCT with RIC	58	32	48 (83)	24 (survivors)	33.6 [†]
Anderlin <i>i et</i> al ³²	Retrospective	Donor leukocyte infusion	27	30	21 (78)	41 (5 survivors)	17.6^{\dagger}

Table 1 Study design and key patient characteristics of 41 identified studies included in the meta-analysis.

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	Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
Inc on 05/11/15				HL patients	years	prior ASCT, <i>n</i> (%)	(months)	from KM curve [†]), month
ls North America	Armand et al ³³	Retrospective	Allo-SCT with RIC	36	31	34 (94)	26 (survivors)	48.3^{\dagger}
akeda Pharmaceutica only	Baron et al ³⁴	Prospective cohort	Allo-SCT following nonmyeloablative conditioning	35/147*	46 (all patients)	NR (~92) (all patients)	26.7 (survivors)	22.3 [†]
lthcare.com by 7 for nersonal use	Bartlett et al ³⁵	Phase 1/2	GVD	91 (40 with previous ASCT)	33 (all patients)	40 (44)	43.2 (survivors)	42
uformaheal F	Blum et al ³⁶	Phase 2	Bortezomib	30	35	24 (80)	18 (all patients)	14.8
rr Med Res Opin Downloaded trom Ir	Burroughs et al ³⁷	Retrospective	Allo-SCT following nonmyeloablative conditioning	90 total HLA-matched: 38 Unrelated: 24 HLA-haploidentical: 28	HLA-matched: 33 Unrelated: 28 HLA-haploidentical: 32	HLA-matched: 34 (89) Unrelated: 24 (100) HLA-haploidentical: 25 (89)	Survivors: HLA-matched: 24 Unrelated: 38 HLA-haploidentical: 22	HLA-matched: 26.4 [†] Unrelated: 46.5 [†] HLA-haploidentical: 47.5 [†]
Cui	Chen et al ³⁸	Retrospective	Allo-SCT with RIC	24	35	20 (83)	27.2 (all patients)	39.6 [†]



Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
			HL patients	years	prior ASCT, <i>n</i> (%)	(months)	from KM curve [†]), month
Clozel et al ³⁹	Retrospective	PLD or PLD+MOPP/GVD/ BEACOPP/vinblastine	47	25	47 (100) [‡]	36	42 [†]
Corazzelli et al ⁴⁰	Retrospective	Bendamustine and allo-	41	33	35 (85)	Not reported	21.4
Corradini et al ⁴¹	Phase 2	Allo-SCT with RIC	32/170*	51 (all patients)	25 (78)	33 (all patients)	26.9^{\dagger}
Czyz et al ⁴²	Retrospective	GCS or GV	37	32	37 (100) [‡]	26.4 (survivors)	15.5
Devetten et	Retrospective	RIC and nonmyeloablative SCT	143	30	127 (89)	25 (survivors)	14.8^{\dagger}
Fehniger et	Phase 2	Lenalidomide	36/38	34	29 (76)	20	20
	Clozel et al ³⁹ Corazzelli et al ⁴⁰ Corradini et al ⁴¹ Czyz et al ⁴² Devetten et al ⁴³ Fehniger et al ⁴⁴	Clozel et alRetrospectiveCorazzelli et alRetrospectiveCorradini et alPhase 2Czyz et alRetrospectiveDevetten et alRetrospectiveCzyz et alRetrospectivePhase 2RetrospectiveDevetten et alRetrospectivePhase 2Retrospective	PLD orClozel et al 39RetrospectivePLD+MOPP/GVD/ BEACOPP/vinblastineCorazzelli et al 40RetrospectiveBendamustine and allo- SCTCorradini et al 41Phase 2Allo-SCT with RICCorzyz et al 42RetrospectiveGCS or GVCzyz et al 42RetrospectiveRIC and nonmyeloablative SCTPenniger et al 44Phase 2Lenalidomide	HL patients HL patients HT pa	HL patients years HL patients years Clozel et al ³⁹ Retrospective PLD-MOPP/GVD/ BEACOPP/vinblastine 47 Corazzelli et al ⁴⁰ Retrospective Bendamustine and allo- SCT 41 Corradini et al ⁴¹ Phase 2 Allo-SCT with RIC 32/170* Str 51 (all patients) Corradini et al ⁴³ Retrospective Retrospective RIC and nonmyeloablative SCT 143 Schinger et al ⁴⁴ Phase 2 Lenalidomide 36/38	HL patients years prior ASCT, r (%) HL patients prior ASCT, r	HL patientsyearsprior ASCT, n (%)(months)Clorel et al. ⁹⁹ RetrospectivePLD or PLD+MOPP/GVD/ BEACOPP/violabatine472547 (100) ² 36Corazzelli et al. ⁹⁰ RetrospectiveBendamustine and allo- SCT413335 (85)Not reportedCorazili et al. ⁹¹ Phase 2Allo-SCT with RIC32/170*51 (all patients)25 (78)33 (all patients)Corazili et al. ⁹¹ RetrospectiveGCS or GV373237 (100) ⁴ 26.4 (survivors)Corazili et al. ⁹¹ RetrospectiveRC and nonnycloablative SCT14330127 (89)25 (survivors)Corazili et al. ⁹¹ Phase 2Lenaldomide36/383429 (76)20



Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
STATE			HL patients	years	prior ASCT, n (%)	(months)	from KM curve [†]), month
a Inc on U5							
Ghesquieres	Retrospective	Bendamustine or					
f_{10}^{4} et al ⁴⁵	studv	bendamustine + rituximab	28	32	25 (89)	16.5	Not reached
euticals N		or vinorelbine					
Goda et al ⁴⁶	Retrospective	Salvage RT or	56	30	56 (100) [‡]	31.3	40.8
only.	study	RT with salvage CT	50	50	30(100)	51.5	40.0
Gopal et al ²²	Pivotal Phase 2	Brentuximab vedotin	102	31	102 (100) [‡]	32.7	40.5
$\overset{1}{\overset{1}{\overset{1}{\overset{1}{\overset{1}{\overset{1}{\overset{1}{\overset{1}$	Phase 2	Perifosine and perifosine	25/40*	42 (all patients)	27 (67) (all patients)	14 (all patients)	16
If ormanea]		+ sorafenib					
Harrison et	Prospective	Panobinostat	129	32	129 (100) [‡]	NA	Not reached
	cohort						
Johansson et						25 (all patients)	*
ido al ⁴⁹	Retrospective	Allo-SCT with RIC	23	36	20 (87)	46 (survivors)	52.1'
Curr							



Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
			HL patients	years	prior ASCT, n (%)	(months)	from KM curve [†]), month
Majhail et al ⁵⁰	Prospective cohort	UCB or MSD allo-SCT with RIC	21 total UCB: 9 MSD:12	UCB: 28 MSD:42	UCB: 7 (78) MSD: 7 (58)	UCB: 17 MSD:24	UCB: Not reached MSD: 16.2 [†]
$\frac{5}{5}$ Marcais et al ⁵¹	Retrospective	Allo-SCT	191	31	174 (92)	36	55
Moskowitz et al ⁵²	Phase 2	Bendamustine	34/36	34	27 (75)	19 (all patients) 36 (survivors)	29^{\dagger}
Peggs et al ⁵³	Prospective cohort	Allo-SCT with RIC	49 total Unrelated donors: 18 Related donors: 31	32	44 (90)	31.8 (survivors)	Unrelated donors: 14 [†] Related donors: Not reached



Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
			HL patients	years	prior ASCT, <i>n</i> (%)	(months)	from KM curve [†]), month
Peggs et al ⁵⁴	Retrospective	Allo-SCT with RIC followed by GvHD prophylaxis with MF-A or MF	67 total MF-A: 31 MF: 36	MF-A: 36 MF: 35	MF-A: 27 (87) MF: 26 (72)	MF-A: 58.6 (survivors) MF: 41.7 (survivors)	MF-A: Not reached MF: 25 [†]
Robinson et al ⁵⁵ al	Retrospective	Allo-SCT with RIC	272/285	31.2	229 (80)	26 (all patients)	28.4 [†]
Sarina et al ⁵⁶	Retrospective	Donor group: conditioning regimen No donor group: salvage chemotherapy or radiotherapy	104	31.9	104 (100) [‡]	47.9 (all patients)	Allo-SCT patients: 37.9 [†]
Schmitz et al ⁵⁷	Retrospective	Nonmyleoablative conditioning + allo-SCT	80/94	30	NR (~50)	NR	18.6^{\dagger}



Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
			HL patients	years	prior ASCT, n (%)	(months)	from KM curve [†]), month
Shamash et al ⁵⁸	Retrospective	HDCT with autologous haematopoietic support	37 total Single sequential chemotherapy: 20 multiple agent group: 17	28	37 (100) [‡]	24	Single sequential chemotherapy: 12.0 multiple agent group: 21.9
smith et al ⁵⁹	Retrospective	Second ASCT	21/40*	38 (all patients)	40 (100) [‡] (all patients)	72 (survivors)	24^{\dagger}
$\stackrel{\overline{b}}{\underline{E}}$ Smith et al ⁶⁰	Phase 2	Galiximab	29/30	36	21 (70)	13.6	23.2
Sobol et al ⁶¹	Prospective cohort	Allo-SCT with RIC	31	36	100‡	84	Chemorefractory bulky: 19.4, Chemorefractory nonbulky: NA, Chemosensitive bulky: 18.4, Chemosensitive nonbulky: NA



Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
a Inc on 05/11/15			HL patients	years	prior ASCT, <i>n</i> (%)	(months)	from KM curve [†]), month
ith Ameri		Allo-SCT with RIC or	168 total		\sim		
5 Z Sureda et al ⁶²	Retrospective	myeloablative	RIC: 89	RIC: 26	RIC: 55 (61.8)	RIC: 73	RIC: 14.6
akeda Pharmaceutica only.	Kenospective	conditioning	Myeloablative:79	Myeloablative:27	Myeloablative: 32 (40.5)	Myeloablative: 76	Myeloablative: 6.7
n by T al use						32 (all patients)	
For Sureda et al ⁶⁵ For person For person F	Phase 2	Allo-SCT with RIC	78/92	28	79 (86)	48 (survivors)	30.1'
Thomson et al ⁶⁴	Phase 2	Allo-SCT with RIC	38	31	38 (100) [‡]	49 (survivors)	46^{\dagger}
Validire et al ⁶⁵	Retrospective	Gemcitabine-based regimen	55	29	34 (62)	14 (all patients)	20.7^{\dagger}
Curr Med Res							





Allo-SCT = allogeneic stem cell transplant; ASCT = autologous stem cell transplant; BEACOPP = bleomycin, etoposide, doxorubicin,

cyclophosphamide, vincristine, procarbazine, and prednisone; CT = chemotherapy; GCS = gemcitabine, cisplatin, and methylprednisolone or dexamethasone;

GV = gemcitabine and vinorelbine; GVD = gemcitabine, vinorelbine, and pegylated liposomal doxorubicin; GvHD = graft versus host disease; HDCT = high

analysis

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dose chemotherapy; MF-A = cyclosporine, alemtuzumab; MF = closporine, methotrexate; MOPP = mechlorethamine, vincristine, procarbazine, prednisone; MSD = matched-sibling donors; NR = not reported; PLD = pegylated liposomal doxorubicin; RIC = reduced-intensity conditioning; RT = radiotherapy; SCT = stem cell transplant; UCB = umbilical cord blood

Table 1 Study design and key patient characteristics of 41 identified studies included in the meta-analysis.

Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
			HL patients	years	prior ASCT, n (%)	(months)	from KM curve [†]), month
Alvarez et al ²⁸	Prospective cohort	Allo-SCT with RIC	40	35	29 (73)	8.5	20^{\dagger}
Anastasia et al ²⁹	Prospective cohort	Bendamustine	69/73	34	73 (100) [‡]	13	Not reached
Anderlini et al ³⁰	Retrospective	Allo-SCT with RIC	40	31	30 (75)	12 (all patients) 13 (survivors)	Not reached
			3				



Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
		HL patients	years	prior ASCT, n (%)	(months)	from KM curve [†]), month
Prospective cohort	Allo-SCT with RIC	58	32	48 (83)	24 (survivors)	33.6 [†]
Retrospective	Donor leukocyte infusion	27	30	21 (78)	41 (5 survivors)	17.6 [†]
Retrospective	Allo-SCT with RIC	36	31	34 (94)	26 (survivors)	48.3^{\dagger}
Prospective cohort	Allo-SCT following nonmyeloablative conditioning	35/147*	46 (all patients)	NR (~92) (all patients)	26.7 (survivors)	22.3 [†]
Phase 1/2	GVD	91 (40 with previous ASCT)	33 (all patients)	40 (44)	43.2 (survivors)	42
Phase 2	Bortezomib	30	35	24 (80)	18 (all patients)	14.8
	Study design Prospective cohort Retrospective Retrospective Prospective cohort Prospective Phase 1/2 Phase 2	Study designRegimenProspective cohortAllo-SCT with RICRetrospectiveDonor leukocyte infusionRetrospectiveAllo-SCT with RICProspective cohortAllo-SCT following nonmyeloablative conditioningPhase 1/2GVDPhase 2Bortezomib	Study designRegimenNumber of evaluableProspective cohortAllo-SCT with RIC58RetrospectiveDonor leukocyte infusion27RetrospectiveAllo-SCT with RIC36Prospective cohortAllo-SCT following nonmyeloablative 	Study designRegimenNumber of evaluableMedian baseline age, HL patientsProspective cohortAllo-SCT with RIC5832RetrospectiveDonor leukocyte infusion2730RetrospectiveDonor leukocyte infusion2730RetrospectiveAllo-SCT with RIC3631Prospective cohortAllo-SCT following nonmyeloablative conditioning35/147*46 (all patients)Phase 1/2GVD91 (40 with previous ASCT)33 (all patients)Phase 2Bortezomib3035	Study designRegimenNumber of evaluableMedian baseline age, yearsNumber of HL patients with prior ASCT, n (%)Prospective cohortAllo-SCT with RIC583248 (83)Retrospective cohortDonor leukocyte infusion273021 (78)Retrospective cohortAllo-SCT with RIC363134 (94)Prospective cohortAllo-SCT with RIC363134 (94)Prospective cohortAllo-SCT following nonmyeloablative conditioning35/147*46 (all patients) Allo all patients)NR (-92) (all patients)Phase 1/2GVD91 (40 with previous ASCT)33 (all patients)40 (44)Phase 2Bortezonub303524 (80)	Study designRegimenNumber of evaluableMedian baseline age, yearsNumber of HL patients with prior ASCT, n (%)Median follow up (months)Prospective cohortAllo-SCT with RIC583248 (83)24 (survivors)Retrospective cohortDonor leukocyte infusion273021 (78)41 (5 survivors)Retrospective cohortAllo-SCT with RIC363134 (94)26 (survivors)Prospective cohortAllo-SCT following nonnyeloablative conditioning35/147*46 (all patients)NR (-92) (all patients)26.7 (survivors)Phase 1/2GVD91 (40) with previous ASCT33 (all patients)40 (44)43.2 (survivors)Phase 2Bortezonib303524 (80)18 (all patients)



Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
			HL patients	years	prior ASCT, <i>n</i> (%)	(months)	from KM curve [†]), month
						$\mathbf{\vee}$	
			90 total			Survivors:	
Burroughs et		Allo-SCT following	HLA-matched: 38	HLA-matched: 33	HLA-matched: 34 (89)	HLA-matched: 24	HLA-matched: 26.4 [†]
al ³⁷	Retrospective	nonmyeloablative	Unrelated: 24	Unrelated: 28	Unrelated: 24 (100)	Unrelated: 38	Unrelated: 46.5
		conditioning	HLA-haploidentical: 28	HLA-haploidentical: 32	HLA-haploidentical: 25 (89)	HLA-haploidentical: 22	HLA-haploidentical: 47.5
Chen et al ³⁸	Retrospective	Allo-SCT with RIC	24	35	20 (83)	27.2 (all patients)	39.6 [†]
ersonal							
Clozel et al ³⁹	Retrospective	PLD or PLD+MOPP/GVD/	47	25	47 (100) [‡]	36	42^{\dagger}
		BEACOPP/vinblastine					
corazzelli et	Retrospective	SCT	41	33	35 (85)	Not reported	21.4
Corradini et al ⁴¹	Phase 2	Allo-SCT with RIC	32/170*	51 (all patients)	25 (78)	33 (all patients)	26.9^{\dagger}



	Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
1/15				HL patients	years	prior ASCT, n (%)	(months)	from KM curve ^{\dagger}), month
a Inc on 05/1								
Americ	Czyz et al ⁴²	Retrospective	GCS or GV	37	32	37 (100) [‡]	26.4 (survivors)	15.5
ls North /	·	·						
eutica	Devetten et	Retrospective	RIC and	143	30	127 (89)	25 (survivors)	14.8^{\dagger}
a Pharmac	al ⁴³	t	nonmyeloablative SCT					
Taked:	Fehniger et	Phase 2	Lenalidomide	36/38	34	29 (76)	20	20
e.com by	al ⁴⁴							
lthcar For ne	Ghesquieres	Retrospective	Bendamustine or					
mahea	et al ⁴⁵	study	bendamustine + rituximab	28	32	25 (89)	16.5	Not reached
from infor		·	or vinorelbine					
aded	Goda et al ⁴⁶	Retrospective	Salvage RT or	56	30	56 (100) [‡]	31.3	40.8
in Downle		study	RT with salvage CT					
d Res Opi	Gopal et al ²²	Pivotal Phase 2	Brentuximab vedotin	102	31	102 (100) [‡]	32.7	40.5
urr Me	Guidetti et al ⁴⁷	Phase 2	Perifosine and perifosine	25/40*	42 (all patients)	27 (67) (all patients)	14 (all patients)	16
Ū			+ sorafenib					



Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
			HL patients	years	prior ASCT, n (%)	(months)	from KM curve [†]), month
Harrison et	Prospective	Panohinostat	120	32	129 (100) [‡]	NA	Not reached
al ⁴⁸	cohort	1 alooniostat	12)	32		NA	
Johansson et						25 (all patients)	
a ¹⁴⁹	Retrospective	Allo-SCT with RIC	23	36	20 (87)		52.1 [†]
а						46 (survivors)	
stronal use of			21 total	\sim			
for pe	Prospective	UCB or MSD allo-SCT		UCB: 28	UCB: 7 (78)	UCB: 17	UCB: Not reached
^{III} Majhail et al ⁵⁰	ht	with DIC	UCB: 9				
	conort	with KIC	MSD:12	MSD:42	MSD: 7 (58)	MSD:24	MSD: 16.2 [†]
51		•					
Marcais et al 31	Retrospective	Allo-SCT	191	31	174 (92)	36	55
Moskowitz et	Phase 2	Bendamustine	34/36	34	27 (75)	19 (all patients)	29^{\dagger}
a_{3}^{32}						36 (survivors)	



Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
			HL patients	years	prior ASCT, <i>n</i> (%)	(months)	from KM curve [†]), month
Peggs et al ⁵³	Prospective cohort	Allo-SCT with RIC	49 total Unrelated donors: 18 Related donors: 31	32	44 (90)	31.8 (survivors)	Unrelated donors: 14 [†] Related donors: Not reached
Peggs et al ⁵⁴	Retrospective	Allo-SCT with RIC followed by GvHD prophylaxis with MF-A or MF	67 total MF-A: 31 MF: 36	MF-A: 36 MF: 35	MF-A: 27 (87) MF: 26 (72)	MF-A: 58.6 (survivors) MF: 41.7 (survivors)	MF-A: Not reached MF: 25 [†]
Robinson et al ⁵⁵	Retrospective	Allo-SCT with RIC	272/285	31.2	229 (80)	26 (all patients)	28.4^{\dagger}
Sarina et al ⁵⁶	Retrospective	Donor group: conditioning regimen No donor group: salvage chemotherapy or radiotherapy	104	31.9	104 (100) [‡]	47.9 (all patients)	Allo-SCT patients: 37.9 [†]



Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
			HL patients	years	prior ASCT, n (%)	(months)	from KM curve [†]), month
Schmitz et al ⁵⁷	Retrospective	Nonmyleoablative conditioning + allo-SCT	80/94	30	NR (~50)	NR	18.6^{\dagger}
			37 total				
Shamash et \therefore al ⁵⁸	Retrospective	HDCT with autologous	Single sequential	28	37 (100) [‡]	24	Single sequential chemotherapy: 12.0
sonal use only			multiple agent group: 17	C/			multiple agent group: 21.9
$\frac{10}{10}$	Patrospactiva	Second ASCT	21/40*	38 (all patients)	40 (100)‡	72 (survivors)	
Shiftir et al	Keuospecuve	Scolu ASCT	21/40	50 (un puronis)	(all patients)	72 (541111013)	24^{\dagger}
Smith et al ⁶⁰	Phase 2	Galiximab	29/30	36	21 (70)	13.6	23.2
							Chemorefractory bulky: 19.4,
Sobol et al ⁶¹	Prospective	ctive Allo-SCT with RIC	31	36	100^{\ddagger}	84	Chemorefractory nonbulky: NA,
	cohort						Chemosensitive bulky: 18.4,
							Chemosensitive nonbulky: NA



Study	Study design	Regimen	Number of evaluable	Median baseline age,	Number of HL patients with	Median follow up	Reported median OS (or derived
a Inc on 05/11/15			HL patients	years	prior ASCT, <i>n</i> (%)	(months)	from KM curve [†]), month
Surada at al ⁶²	Potrognostivo	Allo-SCT with RIC or	168 total RIC: 89	RIC: 26	RIC: 55 (61.8)	RIC: 73	RIC: 14.6
in a sector a marmacceutos	Keuospecuve	conditioning	Myeloablative:79	Myeloablative:27	Myeloablative: 32 (40.5)	Myeloablative: 76	Myeloablative: 6.7
For mean and the second and the seco	Phase 2	Allo-SCT with RIC	78/92	28	79 (86)	32 (all patients) 48 (survivors)	30.1 [†]
Thomson et al ⁶⁴	Phase 2	Allo-SCT with RIC	38	31	38 (100) [‡]	49 (survivors)	46^{\dagger}
Validire et al ⁶⁵	Retrospective	Gemcitabine-based regimen	55	29	34 (62)	14 (all patients)	20.7^{\dagger}
Curt Med Kes							





analysis

Allo-SCT = allogeneic stem cell transplant; ASCT = autologous stem cell transplant; BEACOPP = bleomycin, etoposide, doxorubicin,

cyclophosphamide, vincristine, procarbazine, and prednisone; CT = chemotherapy; GCS = gemcitabine, cisplatin, and methylprednisolone or dexamethasone;

GV = gemcitabine and vinorelbine; GVD = gemcitabine, vinorelbine, and pegylated liposomal doxorubicin; GvHD = graft versus host disease; HDCT = high

dose chemotherapy; MF-A = cyclosporine, alemtuzumab; MF = closporine, methotrexate; MOPP = mechlorethamine, vincristine, procarbazine, prednisone; MSD = matched-sibling donors; NR = not reported; PLD = pegylated liposomal doxorubicin; RIC = reduced-intensity conditioning; RT = radiotherapy; SCT

= stem cell transplant; UCB = umbilical cord blood

