Annals of Hematology (2018) 97:2417–2424
https://doi.org/10.1007/s00277-018-3473-8

ORIGINAL ARTICLE

Posttransplant monomorphic Burkitt's lymphoma: clinical characteristics and outcome of a multicenter series

S. Bobillo[1] · P. Abrisqueta[1] · B. Sánchez-González[2] · E. Giné[3] · S. Romero[4] · M. Alcoceba[5] · E. González-Barca[6] · S. González de Villambrosía[7] · J. M. Sancho[8] · P. Gómez[9] · L. Bento[10] · J. Montoro[1] · S. Montes[11] · A. López[1] · F. Bosch[1] · on behalf of the Grupo Español de Linfomas/Trasplante Autólogo de Médula Ósea (GEL/TAMO cooperative group)

Received: 17 April 2018 / Accepted: 6 August 2018 / Published online: 16 August 2018

Abstract

Burkitt's monomorphic posttransplant lymphoproliferative disorder (B-PTLD) is an uncommon subtype of PTLD. Owing to the paucity of this complication, clinical characteristics and outcome has not been fully described. Clinical characteristics and outcomes of 20 patients diagnosed with B-PTLD from 10 transplant centers belonging to the GEL/TAMO group were reviewed. Median time from transplant to B-PTLD was 7.2 years. All the cases fulfill the morphologic and genetic criteria of B-PTLD, whereas Epstein-Barr virus (EBV) was detected in 70% of cases. Patients were treated with different chemotherapy combinations, and three patients received upfront rituximab monotherapy. The great majority of patients receiving CHOP-like regimens attained a complete response (CR) (73%), similar to that obtained with dose-intensive chemotherapy (83% CR). In contrast, patients receiving upfront rituximab monotherapy required subsequent chemotherapy. Two patients (10%) died during treatment due to infection. The median progression-free survival and overall survival (OS) were 16 months and 139 months, respectively. When analyzing variables predicting for OS, we found that patients with bone marrow involvement had an adverse prognosis, with a median OS of 6 months ($p = 0.008$). In conclusion, B-PTLD is an uncommon complication usually associated with EBV infection and with an aggressive clinical course, particularly in patients with bone marrow involvement. High-dose chemoimmunotherapy obtained similar responses to R-CHOP, suggesting that R-CHOP could be an adequate alternative for these patients. In contrast, rituximab monotherapy does not seem to be effective enough to control the disease.

Keywords Posttransplant lymphoproliferative disorders · Burkitt's lymphoma · Transplantation

Introduction

Posttransplant lymphoproliferative disorders (PTLD) are an unusual complication from the immunosuppressive therapy (IS) administered after hematopoietic stem cell (HSCT) or solid organ transplantation (SOT) [1]. The estimated prevalence of PTLD is 3–5% among patients who underwent SOT, and beneath 1% in those receiving an allogeneic HSCT [2].

✉ F. Bosch
fbosch@vhio.net

[1] Department of Hematology, Vall d'Hebron Institute of Oncology (VHIO), University Hospital Vall d'Hebron, University Autònoma of Barcelona (UAB), Barcelona, Spain

[2] Department of Hematology, Hospital del Mar, Barcelona, Spain

[3] Department of Hematology, Hospital Clínic, Barcelona, Spain

[4] Department of Hematology, Hospital Universitario y Politecnico La Fe, Valencia, Spain

[5] Department of Hematology, Hospital de Salamanca, Salamanca, Spain

[6] Department of Hematology, Institut Català d'Oncologia, L'Hospitalet de Llobregat, Spain

[7] Department of Hematology, Hospital Marqués de Valdecilla, Santander, Spain

[8] Department of Hematology, ICO-IJC-University Hospital Germans Trias i Pujol, Badalona, Spain

[9] Department of Hematology, Hospital La Paz, Madrid, Spain

[10] Department of Hematology, Hospital Universitario Son Espases, Mallorca, Spain

[11] Department of Pathology, Hospital Marqués de Valdecilla, Santander, Spain

From the histological standpoint, PTLDs comprise a wide spectrum of lymphoid and plasmacytic proliferations ranging from Epstein-Barr virus (EBV)-driven polyclonal non-destructive PTLDs to monomorphic lymphomas [3]. More than 70% of PTLD are classified as monomorphic diffuse large B cell lymphoma (DLBCL-PTLD), whereas other subtypes, including Burkitt lymphoma, plasmablastic lymphoma, or multiple myeloma, represent less than 10% [2, 3]. Notably, up to 60% of the PTLD cases are associated with EBV infection [4]. Because of the heterogeneity of these disorders, the paucity of cases, and the variable general condition of the patients, there is no general consensus on the most adequate treatment for PTLD [5, 6]. Decrement of immunosuppression is the usual first approach, which leads to some responses particularly in early lesions or polymorphic variants of the PTLD [7]. The use of rituximab, alone or in combination, significantly improved the outcome of CD20-positive PTLD patients [8, 9]. Albeit this progress, patients presenting with monomorphic variants, advanced stage, or high tumor burden usually require chemotherapy to attain therapeutic response [10–13].

Burkitt lymphoma (BL) is a germinal center-derived mature B cell lymphoma characterized by increased MYC expression, extremely high proliferation rate, and an aggressive clinical course. Three clinical variants of BL are accepted by the World Health Organization (WHO) classification: endemic, sporadic, and immunodeficiency-associated HIV type [14]. Patients usually present with an advanced clinical stage, bulky masses, and extranodal disease, including central nervous system (CNS) involvement [15]. BL has a favorable outcome when treated with high-dose chemoimmunotherapy, including drugs with ability to cross the blood-brain barrier [15]. The drawback of these intensive chemotherapy regimens is their association with high toxicity, particularly in fragile or immunosuppressed patients [16–18]. Lower intensity regimens such as modified EPOCH-R (SC-EPOCH-RR) have been effective in patients with HIV-positive BL [19].

Burkitt lymphoma PTLD (B-PTLD) is an uncommon and aggressive subtype of monomorphic PTLD representing between 3 and 9% of PTLD reported in adult population [3, 20, 21]. Although B-PTLD is generally associated with *MYC* translocation, some cases of B-PTLD with lack of *MYC* translocation and 11q aberrations have been recently described [22]. Due to the reduced number of cases diagnosed with B-PTLD, their clinical characteristics, outcome, and most adequate treatment options are not well established [5, 6, 20–30]. CHOP-like chemotherapy, or Burkitt-like regimens, have obtained adequate response rates [20–30] at the expense of higher treatment-related toxicity and mortality in comparison with BL diagnosed in patients that not underwent transplantation [17, 18, 24].

Owing to the fact that B-PTLD is an infrequent and poorly studied aggressive lymphoma without an optimal treatment approach, we performed a multicenter analysis aimed to provide a better characterization of their clinical characteristics, response to therapy and outcomes of patients diagnosed with B-PTLD.

Material and methods

Patients

Adult patients diagnosed with B-PTLD between February 1996 and April 2015 and belonging to 10 transplant centers from the Grupo Español de Linfomas/Trasplante Autólogo de Médula Ósea (GEL/TAMO cooperative group) were retrospectively identified. Medical records and pathology reports were reviewed to obtain additional information. This study was approved by the ethical committee of the University Hospital Vall d'Hebron.

Histology, Epstein-Barr virus association, and cytogenetic studies

The diagnosis of Burkitt lymphoma was established following the recent criteria established by the World Health Organization classification of hematopoietic and lymphoid tumors [14]. Immunohistochemical data for CD20, CD10, BCL-6, BCL2, MUM-1, and Ki67 were registered. Additionally, information on EBV status by in situ hybridization for Epstein-Barr-encoded small RNA (EBER) was gathered in 13 cases. Compatible fluorescence in situ hybridization (FISH) analysis or conventional karyotype was mandatory to be included in the study. Patients with PTLD negative for *C-MYC* gene breaks and/or positive for *BCL2* or *BCL6* rearrangements by FISH were excluded. Information on conventional karyotype was available in eight patients.

Statistical analysis

Overall survival (OS) was defined as the time from initial diagnosis of B-PTLD to death from any cause. Progression-free survival (PFS) was defined from the date of diagnosis to relapse/progression or death of any cause. Fisher's exact test was used to compare categorical variables. Survival curves were estimated using the Kaplan-Meier method and compared by means of the log-rank test. $P < 0.05$ was considered significant. Cox proportional hazard model was used for multivariable analyses and to obtain hazard ratios (HRs) with 95% confidence intervals (CI 95%). All statistical analyses were performed using STATA version 13.1.

Results

Baseline findings and clinical presentation

Twenty-five adult patients were diagnosed with B-PTLD. Among them, five patients had no cytogenetic studies and therefore were excluded from the analysis. Four patients diagnosed between 1996 and 2002 treated in the pre-rituximab era were included. Starting from January 2003, all patients received rituximab-containing regimens. The main baseline characteristics of the 20 patients are summarized in Table 1. Median age at diagnosis was 45 years (range, 23–71 years), and 11 patients were female (55%). Eighteen patients (90%) underwent solid organ transplantation, being the kidney (n = 11) the most frequent organ transplanted. Two additional patients received an allogeneic stem cell transplant (alloHCT), one from unrelated donor and another from an identical sibling donor. Underlying diseases for the transplant indication consisted of end-stage renal disease, cirrhosis, cystic fibrosis, dilated cardiomyopathy, and chronic myeloid leukemia in the two patients that underwent alloHCT. Median time from transplant to the diagnosis of B-PTLD was 7.2 years (range, 2 months to 21.7 years), with most of the patients (85%) developing B-PTLD later than 1 year after the transplantation. The two patients receiving an alloHCT developed B-PTLD 4 months and 4 years after transplantation, respectively. Of note, all patients were on immunosuppressant treatment when the PTLD was diagnosed.

The majority of patients presented with advanced clinical stage (Ann Arbor stage IV in 16 cases [80%]), and 11 patients (58%) had B symptoms. Enlarged lymph nodes, together with extranodal disease, were the most common clinical presentation (80%). One patient (7%) presented with CNS involvement at diagnosis. Notably, nine patients (50%) had a poor performance status at diagnosis (ECOG > 2), and four patients (20%) were admitted to the intensive care unit (ICU) before starting treatment. Five patients (25%) presented spontaneous tumor lysis syndrome (TLS) at diagnosis, and two out of five patients required hemodiafiltration to manage renal failure.

Immunohistochemical analyses revealed that all cases were CD20+, CD10+, BCL6+, and BCL2 negative and had Ki67 expression > 90%. The *MYC* gene rearrangement was present in all the cases analyzed by FISH (17/17). The three remaining cases in this series exhibit the t(8;14)(q24;q32) translocation by conventional cytogenetic. Regarding the EBV status, in situ hybridization for EBV (EBER) was positive in 9 out of 13 (69%) patients tested.

Treatments and outcome

Immunosuppressive therapy was reduced at the time of the PTLD diagnosis in all patients. Thirteen patients received chemoimmunotherapy: R-CHOP (n = 9), rituximab combined with high-dose chemotherapy including high-dose methotrexate (MTX) and Ara-C (Burkimab regimen [17]) (n = 3), and R-EPOCH (n = 1). Three patients, two of them with Ann Arbor stage I, received rituximab monotherapy (four weekly courses) as frontline treatment. Finally, four patients diagnosed in the pre-rituximab era were treated with CHOP (n = 1), LLA/LB97 protocol [31] (n = 2), and CODOX-M/IVAC (n = 1). Sixteen patients received CNS prophylaxis including intrathecal methotrexate (n = 9), intravenous MTX (n = 1), or both (n = 6).

Sixteen patients (80%) completed the initial treatment, whereas two patients (10%) died because of infectious toxicity (CHOP [n = 1], R-CHOP [n = 1]), and two required treatment discontinuation (R-CHOP) because of cytomegalovirus reactivation and worsening of the general status. Overall response rate (ORR) to frontline treatment was 80%, with 15 of them achieving a complete response (CR) (75%) and one patient attaining a partial response. Eight out of 11 patients (73%) attained CR after CHOP-like regimens, 5 out of 6 (83%) after dose-intensive chemotherapy and 2 out of 3 after rituximab monotherapy. Eight patients relapsed at a median time of 6 months (range, 2 months to 10 years), including all patients treated with rituximab monotherapy. Two patients presented with an isolated CNS relapse. Salvage therapy consisted of Burkitt-like regimens (Burkimab) (n = 3), R-CHOP (n = 1), R-EPOCH (n = 1), and BAM (BCNU, high-dose cytarabine and MTX) plus intrathecal MTX (n = 1). Two patients received palliative treatment because of their poor clinical condition. By these treatments, 4 patients (67%) reached a CR. One patient (10%) died due to pneumonia when receiving Burkimab, and another one died in CR 5 months after the treatment due to pneumonia. After frontline treatment, 3-year PFS and 3-year OS were 45% [95% CI, 26–64%] and 64% [95% CI, 39–81%], and median PFS and OS were 16 months and 137 months, respectively (Fig. 1).

In the univariate analysis for OS, only bone marrow infiltration but not age, performance status, stage of disease, time from transplantation to PTLD, or transplant type had an impact on the OS. Bone marrow involvement retained the statistical significance in the Cox multivariate analysis (Table 2). Thus, B-PTLD with bone marrow involvement showed a median OS of 6 months compared to a median OS not reached in patients without bone marrow infiltration (p = 0.008) (Fig. 2).

Discussion

Herein, we presented a series of B-PTLD, the largest to our knowledge reported to date, confirming that this type of lymphoma is an exceedingly infrequent complication of transplantation. In accordance with previous reports in adult

Table 1 Baseline characteristics of B-PTLD patients

Characteristics	No. (%)
Median age (range), years	45 (23–71)
Male	9 (42)
Transplant type	
Kidney	11 (55)
Liver	3 (15)
Lung	2 (10)
Heart	2 (10)
AlloHCT	2 (10)
Median time from transplantation to PTLD (range), years	7.2 (0.2–21.7)
< 1 year	3 (15)
≥ 1 year	17 (85)
EBV association ($n = 13$)	
EBV associated	9 (69)
Non-EBV associated	4 (31)
Ann Arbor classification	
I	3 (15)
II	1 (5)
III	–
IV	16 (80)
B symptoms ($n = 18$)	11 (58)
Serum lactate dehydrogenase	
Elevated	19 (95)
Serum β_2 microglobulin ($n = 15$)	
Elevated	10 (67)
Extranodal disease	16 (80)
GI	9 (60)
Liver	1 (7)
Lung	4 (27)
Bone marrow	6 (37)
Breast	1 (7)
CNS	1 (7)
≥ 2 extranodal sites	11 (73)
Bulky mass (> 7 cm)	11 (55)
ECOG performance status ($n = 18$)	
0–1	8 (45)
≥ 2	10 (55)
Spontaneous TLS	
Yes	5 (25)

AlloHCT, allogeneic stem cell transplantation; *B-PTLD*, posttransplantation lymphoproliferative Burkitt's lymphoma; *EBV*, Epstein-Barr virus; *GI*, gastrointestinal; *CNS*, central nervous system; *ECOG*, Eastern Cooperative Oncology Group; *TLS*, tumor lysis syndrome

population [3–6, 8, 10, 12, 13, 20, 21], B-PTLD represents only the 8% of all PTLD in our series.

The histological characteristics of B-PTLD resemble to that described in BL cases not related to transplant [14]. Notably, the observed EBV expression (69%) appears higher than the one reported in sporadic and immunodeficiency-associated HIV BL subtypes (30–40%), and similar to the endemic subtype and to the previously reported B-PTLD series (80%) [20–23]. This is in agreement with the potential role of the EBV infection in the pathogenesis of B-PTLD [20–30]. It seems that this subtype of lymphoma is a late complication of the transplantation, with a median time of 7.2 years. These figures are similar to previously reported B-PTLD cases and to DLBCL-PTLD, pointing out that B-PTLD is probably a

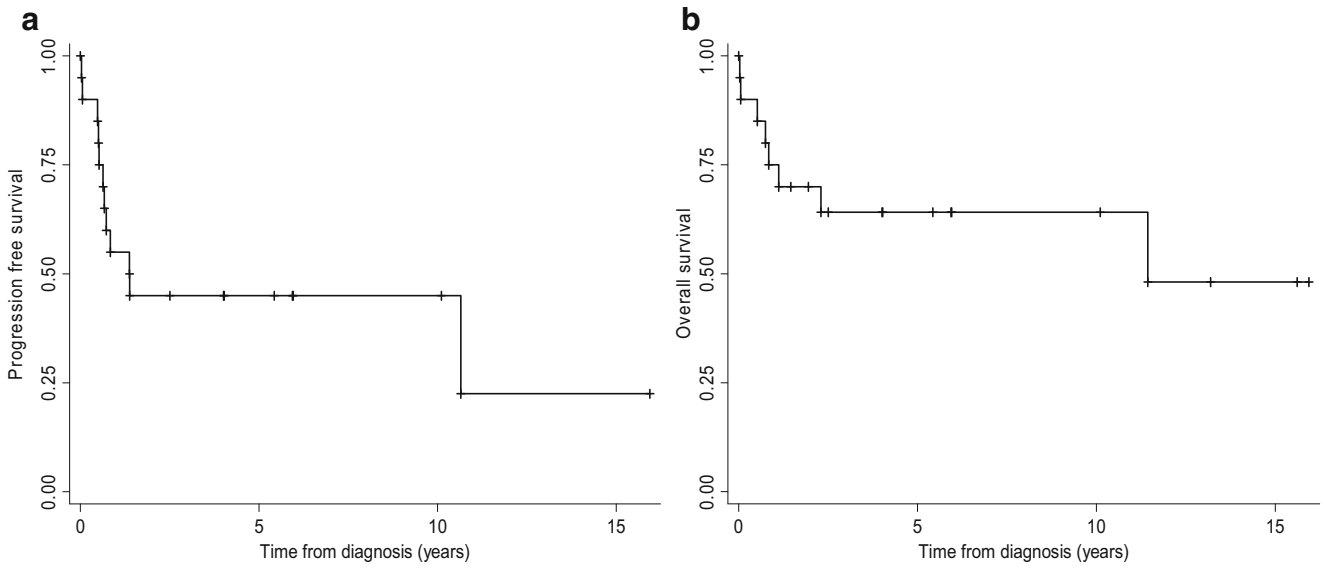

Fig. 1 Progression-free survival and overall survival curves of all patients diagnosed with B-PTLD ($n = 20$). **a** Progression-free survival of all patients. The 3-year estimate PFS was 45% [95% CI, 26–64%]. **b** Overall survival of all patients. The 3-year estimate OS was 64% [95% CI, 39–81%]

complication of a very prolonged immunosuppression [20–30]. However, it should be noted that in our series, one of two patients receiving alloHCT developed B-PTLD 4 months after transplantation in accordance with previously described in alloHCT-related PTLD [32].

Clinical presentation features of B-PTLD in our series included advanced stage, B symptoms, and frequent extranodal involvement, alike to what is described in other BL subtypes [15]. It should be noted that B-PTLD is an extremely aggressive lymphoma at diagnosis; thus, in our series 10 patients (50%) presented with poor performance status (ECOG 3 or 4), 4 patients (20%) required ICU admission before treatment, and 5 patients (25%) had tumor lysis syndrome (TLS) at diagnosis. Strikingly, 2 out of 5 patients required hemodiafiltration to manage renal failure, confirming TLS is a serious complication among B-PTLD patients probably increased by the presence of basal renal injury due to IS [33].

A high response rate has been reported in B-PTLD with different approaches, ranging from high-dose chemotherapy and CHOP-like regimens to rituximab monotherapy [20–30]. In our series, most patients received chemotherapy with (65%) or without rituximab (20%) as frontline treatment. Even though R-CHOP is a suboptimal treatment for BL [34], we observed a CR rate of 73% after CHOP or R-CHOP, similar to dose-intensive regimens (CR 83%) ($p = 0.62$). A few cases of B-PTLD responding to rituximab monotherapy have also been described among the pediatric population. However, this approach did not result in long-term remission in adult patients with aggressive PTLD, with a median PFS of 6 months and 2-year OS of 51% [10]. In our series, patients treated with rituximab monotherapy required further chemotherapy, including two patients at early stage disease, suggesting that addition of chemotherapy is needed to control this aggressive lymphoma, even at early stages.

Table 2 Predictive factors of overall survival, multivariate analysis (Cox proportional hazard model)

Variable	Hazard ratio	95% confidence interval	*p* value
Age			
< 45 vs. ≥ 45	1.621	0.269–9.769	0.598
Performance status			
≤ 2 vs. > 2	0.949	0.157–5.742	0.955
Time from transplantation			
Early vs. late PTLD	0.45	0.044–4.624	0.502
Stage of disease			
Limited (Ann Arbor I/II) vs. advanced (Ann Arbor III/IV)	0.612	0.05–7.439	0.7
Bone marrow involvement	6.538	1.110–38.510	0.038

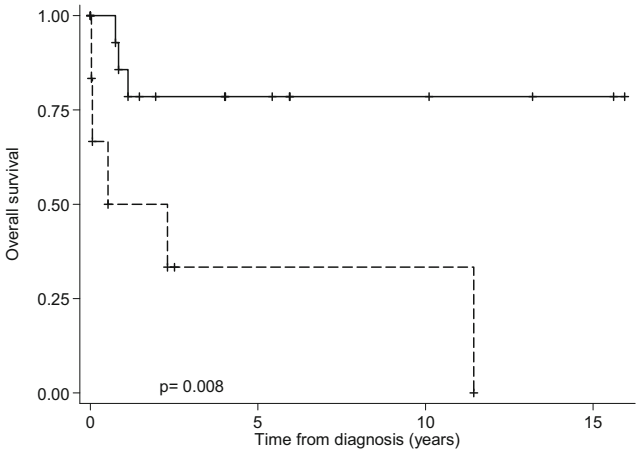

Fig. 2 Patients with B-PTLD and bone marrow involvement ($n = 6$, dashed line) have an inferior overall survival (median OS 6 months) than those without bone marrow infiltration ($n = 14$, solid line) (median OS not reached)

Despite the aggressive clinical course of B-PTLD, we observed a prolonged OS with a median OS of 137 months, which suggests that both R-CHOP and more intensive chemotherapy combinations could be suitable for B-PTLD. After analyzing different clinical variables, the only factor associated with poor survival was the bone marrow involvement, with a median OS of only 6 months, in line with previously observed in BL [35].

The toxicity and mortality related to chemotherapy have been a concern in the posttransplant setting [12, 13]. High-intensive regimens have shown a treatment-related mortality (TRM) of 60% in a series of 5 B-PTLD patients in the pre-rituximab era [24]. Less intensive therapies, such as R-CHOP, have been associated with apparently less toxicity than high-intensive regimens [21]. In our study, we observed two treatment-related deaths and two patients who needed treatment discontinuation. Recently, the German PTLD Study Group and the European PTLD Network reported the high efficacy of sequential treatment with rituximab followed by CHOP in CD20-positive PTLD with less toxic effects and lower TRM than conventional R-CHOP [12, 13]. The same authors retrospectively evaluated the outcome of 5 B-PTLD patients treated with this sequential approach. They observed 80% of complete responses (4/5) with no TRM and an apparently good safety profile [21], although, due to the reduced number of B-PTLD included, the potential role of the sequential treatment remains unclear.

Another issue in B-PTLD management is the need for CNS prophylaxis. Several cases of B-PTLD with an early CNS relapse have been reported so far [6, 21]. Notably, most of them had not received prophylaxis. In our series, 80% of patients were treated with intravenous or intrathecal MTX, and 2 patients presented CNS relapse (10%). Thus, our data favors the use of CNS prophylaxis in patients with B-PTLD, either intrathecal or using systemic drugs which cross the blood-brain barrier.

In conclusion, in this series, B-PTLD behaves like an aggressive subtype of PTLD, especially in patients with bone marrow infiltration, and is usually associated with EBV infection. Chemoimmunotherapy combinations, including Burkitt-based therapies and less intensive regimens such as R-CHOP or low intensity R-EPOCH-based treatments, can obtain a good response in B-PTLD. For patients who are not candidate to intensive regimens, R-CHOP-like regimens seem to be an adequate alternative. Furthermore, rituximab alone does not seem to be effective even in early stages.

Contribution All the authors contributed to the writing, approval, and review of the manuscript.

Compliance with ethical standards

Conflict of interest Dr. Francesc Bosch disclosures:
Research support: Roche, Gilead, Janssen, Celgene, Novartis, Abbvie, Takeda Honoraria (speaker's bureau and/or advisory board): Roche, Gilead, Janssen, Celgene, Abbvie, and Takeda.

Ethical approval This study was approved by the ethical committee of the University Hospital Vall d'Hebron.

References

1. Penn I, Hammond W, Brettschneider L, Starzl TE (1969) Malignant lymphomas in transplantation patients. Transplant Proc 1:106–112
2. Dierickx D, Tousseyn T, Sagaert X, Fieuws S, Wlodarska I, Morscio J, Brepoels L, Kuypers D, Vanhaecke J, Nevens F, Verleden G, van Damme-Lombaerts R, Renard M, Pirenne J, de Wolf-Peeters C, Verhoef G (2013) Single-center analysis of biopsy-confirmed posttransplant lymphoproliferative disorder: incidence, clinicopathological characteristics and prognostic factors. Leuk Lymphoma 54(11):2433–2440
3. Swerdlow SH, Webber SA, Chadburn A, Ferry JA (2016) Post-transplant lymphoproliferative disorders. In: Swerdlow SH, Campo E, Harris NL et al (eds) WHO classification of tumours of haematopoietic and lymphoid tissues, Revised 4th edn. International Agency for Research on Cancer, Lyon, France, pp 453–462
4. Luskin MR, Heil DS, Tan KS, Choi S, Stadtmauer EA, Schuster SJ, Porter DL, Vonderheide RH, Bagg A, Heitjan DF, Tsai DE, Reshef R (2015) The impact of EBV status on characteristics and outcomes of posttransplantation lymphoproliferative disorders. Am J Transplant 15(10):2665–2673
5. Parker A, Bowles K, Bradley JA, Emery V, Featherstone C, Gupte G, Marcus R, Parameshwar J, Ramsay A, Newstead C, On behalf of the Haemato-oncology Task Force of the British Committee for Standards in Haematology and British Transplantation Society (2010) Management of post-transplantation lymphoproliferative disorder in adult solid organ transplant recipients- BCSH and BTS guidelines. Br J Hematol 149(5):693–705
6. Dierickx D, Tousseyn T, Gheysens O (2015) How I treat posttransplant lymphoproliferative disorders. Blood 126(20): 2274–2283

7. Reshef R, Vardhanabhuti S, Luskin MR, Heitjan DF, Hadjiliadis D, Goral S, Krok KL, Goldberg LR, Porter DL, Stadtmauer EA, Tsai DE (2011) Reduction of immunosuppression as initial therapy for posttransplantation lymphoproliferative disorder. Am J Transplant 11(2):336–347
8. Choquet S, Leblond V, Herbrecht R, Socié G, Stoppa AM, Vandenberghe P, Fischer A, Morschhauser F, Salles G, Feremans W, Vilmer E, Peraldi MN, Lang P, Lebranchu Y, Oksenhendler E, Garnier JL, Lamy T, Jaccard A, Ferrant A, Offner F, Hermine O, Moreau A, Fafi-Kremer S, Morand P, Chatenoud L, Berriot-Varoqueaux N, Bergougnoux L, Milpied N (2006) Efficacy and safety of rituximab in B-cell-posttransplantation lymphoproliferative disorders: results of a prospective multicenter phase II study. Blood 107(8):3053–3057
9. Oertel SH, Verschuuren E, Reinke P et al (2005) Effect of anti-CD20 antibody rituximab in patients with post-transplant lymphoproliferative disorder (PTLD). Am J Transplant 5(12):2901–2906
10. Choquet S, Oertel S, LeBlond V, Riess H, Varoqueaux N, Dörken B, Trappe R (2007) Rituximab in the management of post-transplantation lymphoproliferative disorder after solid organ transplantation: proceed with caution. Ann Hematol 86(8):599–607
11. González-Barca E, Domingo-Domenech E, Capote FJ, Gómez-Codina J, Salar A, Bailen A, Ribera JM, López A, Briones J, Muñoz A, Encuentra M, de Sevilla AF, GEL/TAMO (Grupo Español de Linfomas), GELCAB (Grupo para el Estudio de los Linfomas Catalano-Balear), GOTEL (Grupo Oncológico para el Tratamiento y Estudio de los Linfomas) (2007) Prospective phase II trial of extended treatment with rituximab in patients with B-cell post-transplant lymphoproliferative disease. Hematologica 92(11): 1489–1494
12. Trappe RU, Oertel S, Leblond V, Mollee P, Sender M, Reinke P, Neuhaus R, Lehmkuhl H, Horst HA, Salles G, Morschhauser F, Jaccard A, Lamy T, Leithäuser M, Zimmermann H, Anagnostopoulos I, Raphael M, Riess H, Choquet S, German PTLD Study Group, European PTLD Network (2012) Sequential treatment with rituximab followed by CHOP chemotherapy in adult B-cell posttransplant lymphoproliferative disorder (PTLD): the prospective international multicentre phase 2 PTLD-1 trial. Lancet Oncol 13(2):196–206
13. Trappe RU, Dierickx D, Zimmermann H et al (2017) Response to rituximab induction is a predictive marker in B-cell post-transplant lymphoproliferative disorder and allows successful stratification into rituximab or R-CHOP consolidation in an international, prospective, multicenter phase II trial. J Clin Oncol 35(5):536–543
14. Leoncini L, Campo E, Stein H, Harris NL, Jaffe ES, Kluin PM (2016) Burkitt lymphoma. In: Swerdlow SH, Campo E, Harris N et al (eds) WHO classification of tumours of haematopoietic and lymphoid tissues, Revised 4th edn. International Agency for Research on Cancer, Lyon, pp 330–334
15. Linch DC (2012) Burkitt lymphoma in adults. Br J Haematol 156(6):693–703
16. Corazzelli G, Frigeri F, Russo F, Frairia C, Arcamone M, Esposito G, de Chiara A, Morelli E, Capobianco G, Becchimanzi C, Volzone F, Saggese M, Marcacci G, de Filippi R, Vitolo U, Pinto A (2012) RD-CODOX-M/IVAC with rituximab and intrathecal liposomal cytarabine in adult Burkitt lymphoma and 'unclassifiable' highly aggressive B-cell lymphoma. Br J Haematol 156(2):234–244
17. Ribera JM, Garcia O, Grande C et al (2013) Dose-intensive chemotherapy including rituximab in Burkitt's leukemia or lymphoma regardless of human immunodeficiency virus infection status. Cancer 119(9):1660–1668
18. Thomas DA, Faderl S, O'Brien S et al (2006) Chemoimmunotherapy with hyper-CVAD plus rituximab for the treatment of adult Burkitt and Burkitt-type lymphoma or acute lymphoblastic leukemia. Cancer 106(7):1569–1580
19. Dunleavy K, Pittaluga S, Shovlin M, Steinberg SM, Cole D, Grant C, Widemann B, Staudt LM, Jaffe ES, Little RF, Wilson WH (2013) Low-intensity therapy in adults with Burkitt's lymphoma. N Engl J Med 369(20):1915–1925
20. Pasquale MA, Weppler D, Smith J, Icardi M, Amador A, Gonzalez M, Kato T, Tzakis A, Ruiz P (2002) Burkitt lymphoma variant of post-transplant lymphoproliferative disease (PTLD). Pathol Oncol Res 8(2):105–108
21. Zimmermann H, Reinke P, Neuhaus R, Lehmkuhl H, Oertel S, Atta J, Planker M, Gärtner B, Lenze D, Anagnostopoulos I, Riess H, Trappe RU (2012) Burkitt post-transplantation lymphoma in adult solid organ transplant recipients: sequential immunochemotherapy with rituximab (R) followed by cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or R-CHOP is safe and effective in an analysis of 8 patients. Cancer 118(19):4715–4724
22. Ferreiro JF, Morscio J, Dierickx D, Marcelis L, Verhoef G, Vandenberghe P, Tousseyn T, Wlodarska I (2015) Post-transplant molecularly defined Burkitt lymphomas are frequently MYC-negative and characterized by the 11q-gain/loss pattern. Haematologica 100:e275
23. Picarsic J, Jaffe R, Mazariegos G, Webber SA, Ellis D, Green MD, Reyes-Múgica M (2011) Post-transplant Burkitt lymphoma is a more aggressive and distinct form of post-transplant lymphoproliferative disorder. Cancer 117(19):4540–4550
24. Xicoy B, Ribera J-M, Esteve J, Brunet S, Sanz MA, Fernández-Abellán P, Feliu E (2003) Post-transplant Burkitt's leukemia or lymphoma. Study of 5 cases treated with specific intensive therapy (PETHEMA ALL-3/97 trial). Leuk Lymphoma. 44(9):1541–1543
25. Gong JZ, Stenzel TT, Bennett ER, Lagoo AS, Dunphy CH, Moore JO, Rizzieri DA, Tepperberg JH, Papenhausen P, Buckley PJ (2003) Burkitt lymphoma arising in organ transplant recipients: a clinicopathologic study of 5 cases. Am J Surg Pathol 27(6):818–827
26. Hunt BJ, Thomas JA, Buke M et al (1996) Epstein-Barr virus associated Burkitt lymphoma in a heart transplant recipient. Transplantation 62(6):869–872
27. Stravodimou A, Cairoli A, Rausch T et al (2012) PTLD Burkitt lymphoma in a patient with remote lymphomatoid granulomatosis. Case Rep Med 2012:239719
28. Law MF, Chan HN, Leung C (2014) Burkitt-like post-transplant lymphoproliferative disorder (PTLD) presenting with breast mass in a renal transplant recipient: a report of a rare case. Ann Hematol 93(12):2083–2085
29. Huang Q, Popplewell L, Lu Y, Slovak ML, Forman SJ (2010) Late onset of EBV-driven PTLD/Burkitt lymphoma/leukemia in a patient 10 years after allogenic stem cell transplant for AML. Bone Marrow Transplant 45(1):191–194
30. Seema N, Tayapongsak K, Robbins K et al (2013) Burkitt's lymphoma presenting as a late-onset posttransplant lymphoproliferative disorder following kidney and pancreas transplantation: case repost and review of the literature. Case Rep Oncol 6(1):6–14
31. Oriol A, Ribera JM, Esteve J, Sanz MA, Brunet S, Garcia-Boyero R, Fernández-Abellán P, Martí JM, Abella E, Sánchez-Delgado M, Peñarrubia MJ, Besalduch J, Moreno MJ, Borrego D, Feliu E, Ortega JJ, PETHEMA Group, Spanish Society of Hematology (2003) Lack of influence of human immunodeficiency virus infection status in the response to therapy and survival of adult patients with mature B-cell lymphoma or leukemia. Results of the PETHEMA_LAL3/97 study. Haematologica 88(4):445–453
32. Loren W, Porter DL, Stadtmauer EA et al (2003) Post-transplant lymphoproliferative disorder: a review. Bone Marrow Transplant 31(3):145–155
33. Darmon M, Vincent F, Camous L et al (2013) Tumour lysis syndrome and acute kidney injury in high-risk haematology patients in the rasburicase era. A prospective multicentre study from the Groupe de Recherche en Reanimation Respiratoire et Onco-Hematologique. Br J Haematol 162(4):489–497

34. Smeland S, Blystad AK, Kvaloy SO et al (2004) Treatment of Burkitt's/Burkitt-like lymphoma in adolescents and adults: a 20-year experience from the Norwegiam Radium Hospital with the use of 3 successive regimens. Ann Oncol 15(7):1072–1078
35. Ribera JM, García O, Grande C, Esteve J, Oriol A, Bergua J, González-Campos J, Vall-llovera F, Tormo M, Hernández-Rivas JM, García D, Brunet S, Alonso N, Barba P, Miralles P, Llorente A, Montesinos P, Moreno MJ, Hernández-Rivas JÁ, Bernal T (2013) Dose-intensive chemotherapy, including rituximab in Burkitt's leukemia or lymphoma regardless of human immunodeficiency virus infection status: final results of a phase 2 study (Burkimab). Cancer 119(9):1660–1668