Hodgkin lymphoma arising in patients with chronic lymphocytic leukemia: outcomes from a large multi-center collaboration

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Supplemental Tables

Supplementary Table 1. Number of Patients Identified at Each Site (Listed According to Number of Patients Contributed)	
Site	**# of Patients**
Mayo Clinic	25
Ohio State University	19
Dana Farber Cancer Institute	14
Fred Hutch Cancer Center	6
Duke University	5
Swedish Cancer Institute	5
University of Chicago	5
University of Pennsylvania	5
Cleveland Clinic	4
Thomas Jefferson University	2
University of Utah	2
Oregon Health Science University	1
University of Michigan	1
Total	*94*

Supplementary Table 2. List of Data Variables Collected for Patients with Chronic Lymphocytic Leukemia (CLL) with Transformation to Hodgkin Lymphoma (HL)
Sex
Age at CLL diagnosis
Rai Stage at CLL diagnosis
IGVH Mutational Status/Stereotype
FISH for del13q, tri12, del11q, del17p at CLL diagnosis
B2 microglobulin at CLL diagnosis
Presence of complex karyotype at CLL diagnosis
TP53 status at CLL diagnosis
Name of CLL Therapies and Age at initiation of Therapy
Age at Hodgkin's diagnosis
HT Subtype (I/II)
Ann Arbor stage at HL Diagnosis
ECOG Performance Status at HL Diagnosis
B symptoms at HL Diagnosis
Laboratory Values at HL Diagnosis: • Lactate dehydrogenase • White blood cell count • Absolute lymphocyte Count • Hemoglobin • Platelet • Creatinine • Albumin • Erythrocyte sedimentation rate
Size of Largest lymph node at HL diagnosis
FISH for del13q, tri12, del11q, del17p at HL diagnosis
Presence of complex karyotype at HL diagnosis
HL subtype (nodular sclerosing, mixed cellularity, lymphocyte rich, lymphocyte depleted)
Presence of Epstein Barr Virus in HL cells
Name of HL Therapies and Age at Initiation of Therapy
Radiation Therapy Used and Age at Therapy
Autologous or Allogenetic Hematopoietic Cell Transplantation Performed and Age of Therapy
Age at Last Follow Up
Age at Death if Deceased

Supplemental Table 3. International Prognostic Score for Hodgkin Lymphoma[12]
One point is given for each of the characteristic below. Total score ranges from 0-7.
Absolute lymphocyte count < 0.6 x 10^9/L and/or < 8% of total white blood cell count
Age > 45 years
Hemoglobin < 10.5 g/dL
Male gender
Serum albumin < 4 g/dL
Stage IV disease
White blood cell count ≥ 15 x 10^9/L

Supplemental Table 4. Richter Scoring System[1]
One point is given for each of the characteristic below. Total score ranges from 0-5.
ECOG performance status > 1
Lactate dehydrogenase > 1.5 times upper limit of normal
Platelet count < 100 x 10^9/L
Prior therapy > 1
Tumor size ≥ 5 cm

Supplemental Table 5. Regimens for Frontline Treatment of Hodgkin Transformation	
Regimen	Number (%) N = 94
ABVD-Based	**62 (61)**
ABVD	45 (48)
ABVD + Rituximab	1 (1)
ABVD + Obinutuzumab	1 (1)
AVD-Based	
AVD	5 (5)
AV	1 (1)
AVD + Rituximab	3 (3)
AVD + Ibrutinib	4 (4)
AVD + Rituximab + Acalabrutinib	1 (1)
Brentuximab Vedotin-Based	**10 (11)**
AVD + Brentuximab vedotin	1 (1)
Brentuximab vedotin	7 (7)
Brentuximab vedotin + Rituximab	1 (1)
Brentuximab vedotin + Nivolumab	1 (1)
RCHOP-Based	**7 (7)**
BCVPP	**3 (3)**
Bendamustine + Rituximab	**1 (1)**
ICE	**1 (1)**
Etoposide	**1 (1)**
Vinblastine/Chlorambucil	**1 (1)**
Rituximab	**1 (1)**
Radiation	**1 (1)**
No therapy	**6 (6)**
ABVD = adriamycin, bleomycin, vinblastine, and dacarbazine; RCHOP = rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; BCVPP = carmustine, cyclophosphamide, vinblastine, procarbazine, and prednisone	

Supplemental Table 6. Description of Salvage Regimens Received by HT Patients Relapsing after First Line of Therapy					
ID	HL Treatment #1	HL Treatment #2	HL Treatment #3	HL Treatment #4	HL Treatment #5
A	ABVD	ABVD	BCVPP	BR	BR
B	ABVD	BeGeV			
C	ABVD	BR			
D	ABVD	Brentuximab			
E	ABVD	Brentuximab	BCVPP	MACE-CytaBOM	
F	ABVD	GND	Bendamustine	ICE	
G	ABVD	ICE			
H	ABVD	ICE			
I	ABVD	ICE	Brentuximab		
J	ABVD	ICE	Brentuximab + Bendamustine		
K	ABVD	ICE	GVD	Brentuximab	Nivolumab
L	ABVD	Nivo	Brentuximab	BR	
M	ABVD	RGVP			
N	ABVD + obinutuzumab	ICE			
O	AV	Nivolumab	Brentuximab	PEC	
P	AVD	Brentuximab			
Q	AVD+ ibrutinib	Nivolumab + ibrutinib	Brentuximab		
R	BCVPP	Brentuximab	ABVD	GVP	
S	BR	Rituximab + ICE			
T	Brentuximab	AVD	Bendamustine		
U	Brentuximab	GND			
V	Brentuximab + rituximab	ABVD			
W	CHOP	GN			
X	CHOP	RGDP	RICE	EBV-directed cytotoxic T-lymphocytes	
Y	GND	Nivolumab	Brentuximab		
Z	ICE	Rituximab			
AA	RCHOP	Trial bendamustine , ofatumumab, carboplatin, etoposide			
BB	R-miniCHOP	Brentuximab	Pembrolizumab		
CC	Vinblastine/chlorambucil	Brentuximab	GVP	Vinblastine	

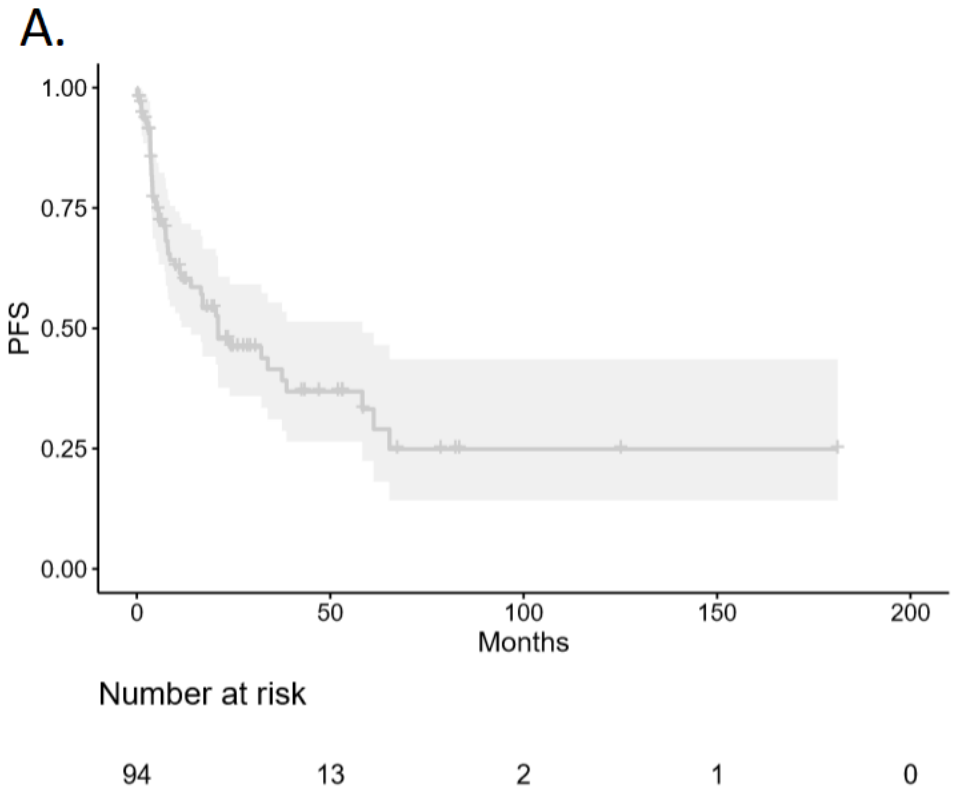
ABVD = adriamycin, bleomycin, vinblastine, and dacarbazine; BCVPP = carmustine, cyclophosphamide, vinblastine, procarbazine, and prednisone; BeGeV = bendamustine, gemcitabine, vinorelbine; BR = bendamustine and rituximab; EBV = Epstein Barr Virus; GDP = gemcitabine, dexamethasone, cisplatin; GND = gemcitabine, navelbine, doxorubicin; GVP = Gemcitabine, vinorelbine, prednisone; ICE = ifosfamide, carboplatin, etoposide; MACE-CytaBOM = cyclophosphamide, doxorubicin, etoposide, cytozar, bleomycin, vincristine, methotrexate and prednisone; PEC = prednisone, etoposide, cyclophosphamide; RCHOP = rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone

Supplemental Table 7. Statistical Significance of Cox Analysis of Overall Survival Based on First Hodgkin Transformation Treatment Before and After Adjusting for Age		
First Therapy for Hodgkin Transformation	**p-value After Adjusting for Age**	**p-value After Adjusting for Age**
ABVD- Full	(Reference Group)	(Reference Group)
ABVD-Reduced	0.043	0.048
Brentuximab	0.054	0.052
No Treatment	0.00004	0.0001
Other	0.00004	0.0002
RCHOP	0.481	0.48
ABVD = adriamycin, bleomycin, vinblastine, and dacarbazine; RCHOP = rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; Other = See supplemental Table 5 for full description of the included regimens		

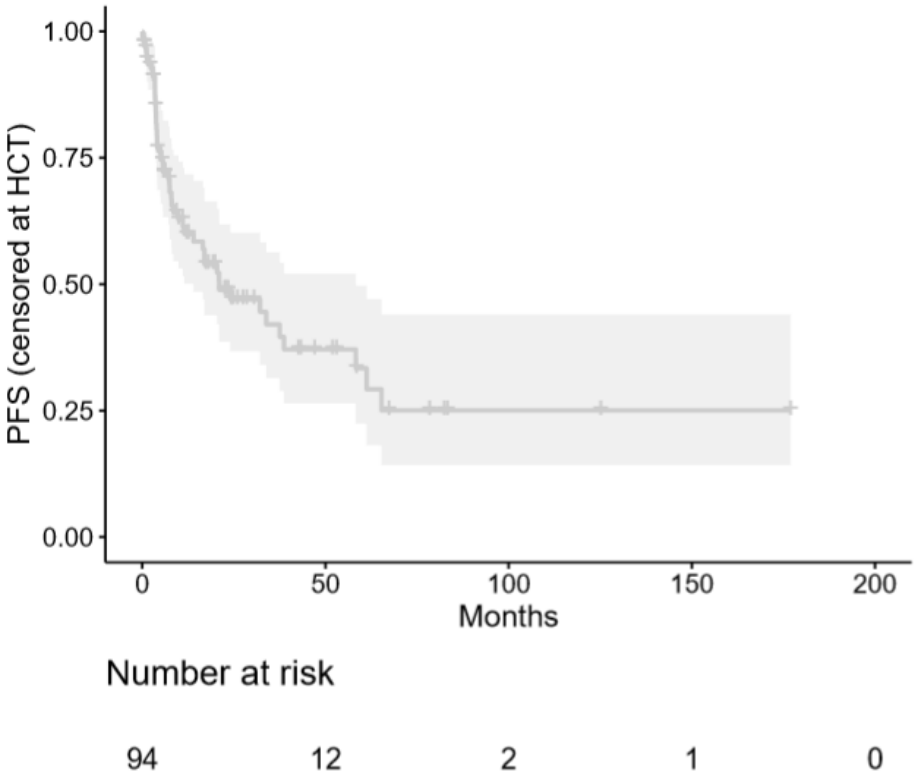
Supplemental Figures

Supplemental Figure Legends

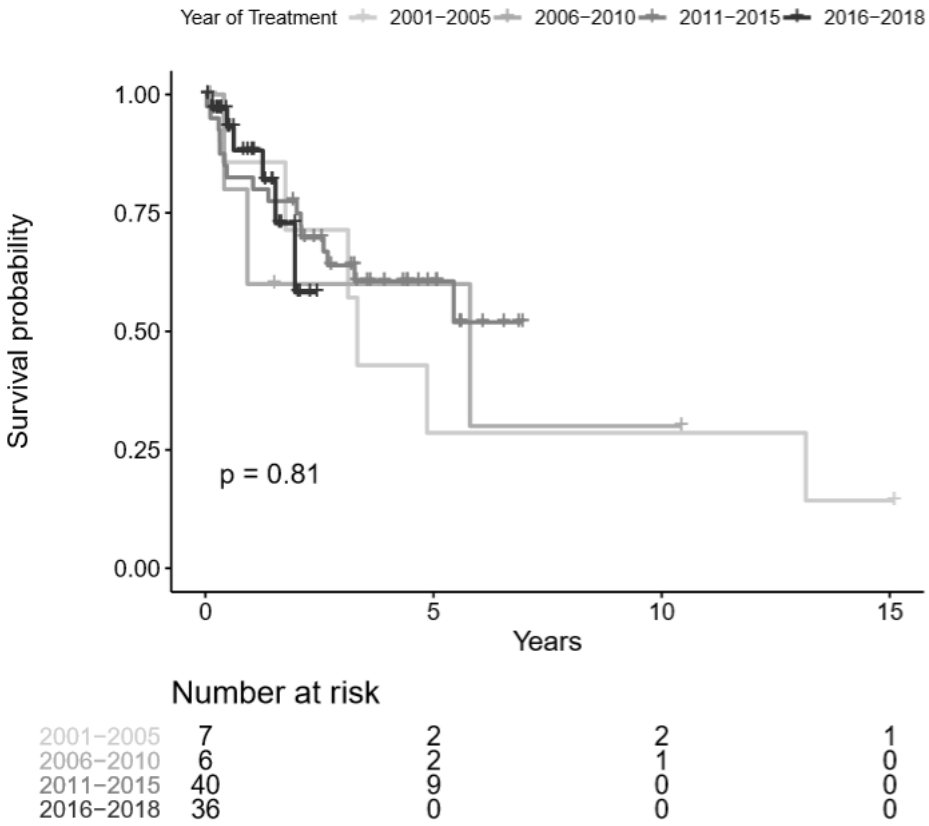
Supplemental Figure 1. (A) Progression-free survival (PFS) for patients with Hodgkin Transformation (HT) without censoring at time of hematopoietic stem cell transplant (HCT). 2-year PFS 48%, 95% CI 38% - 61% (B) PFS for patients with Hodgkin Transformation (HT) without censoring at time of hematopoietic stem cell transplant (HSCT). 2-year PFS = 48.9%, 95% CI 38.7 – 61.8%.



B.


1.00
0.75
0.50
0.25
0.00
PFS (censored at HCT)
0
50
100
150
200
Months
Number at risk
94
12
2
1
0

Supplemental Figure 2. Overall survival for patients with Hodgkin Transformation (HT) based on year of first HT therapy.



Supplemental Figure 3. Overall survival for patients with Hodgkin Transformation based on prior chronic lymphocytic leukemia-directed therapies. BTKi = Bruton's tyrosine kinase inhibitor. Purine = purine analogue therapy.