

# Plasmablastic lymphoma

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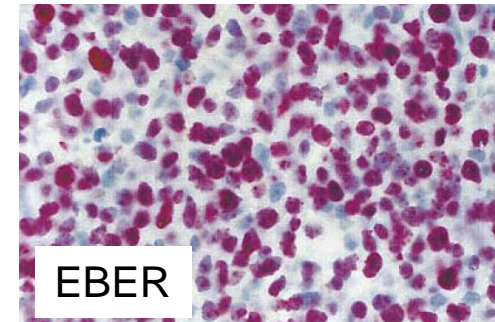
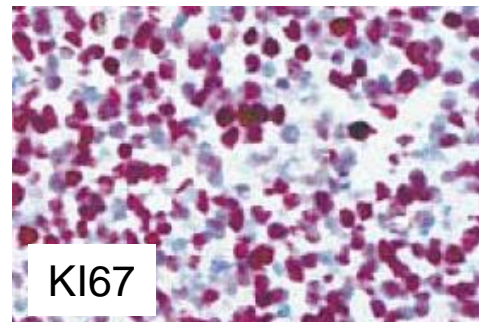
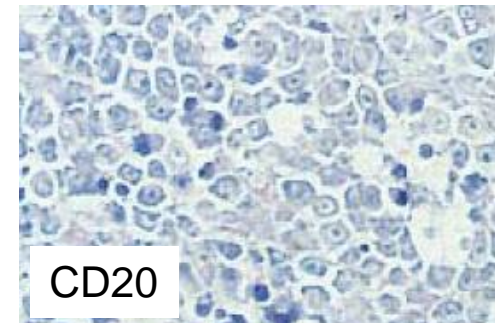
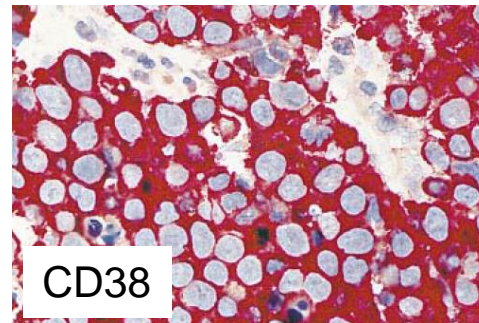
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# Plasmablastic Lymphomas of the Oral Cavity: A New Entity Associated With the Human Immunodeficiency Virus Infection

By H.J. Delecluse, I. Anagnostopoulos, F. Dallenbach, M. Hummel, T. Marafioti, U. Schneider, D. Huhn, A. Schmidt-Westhausen, P.A. Reichart, U. Gross, and H. Stein

## Patients' characteristics

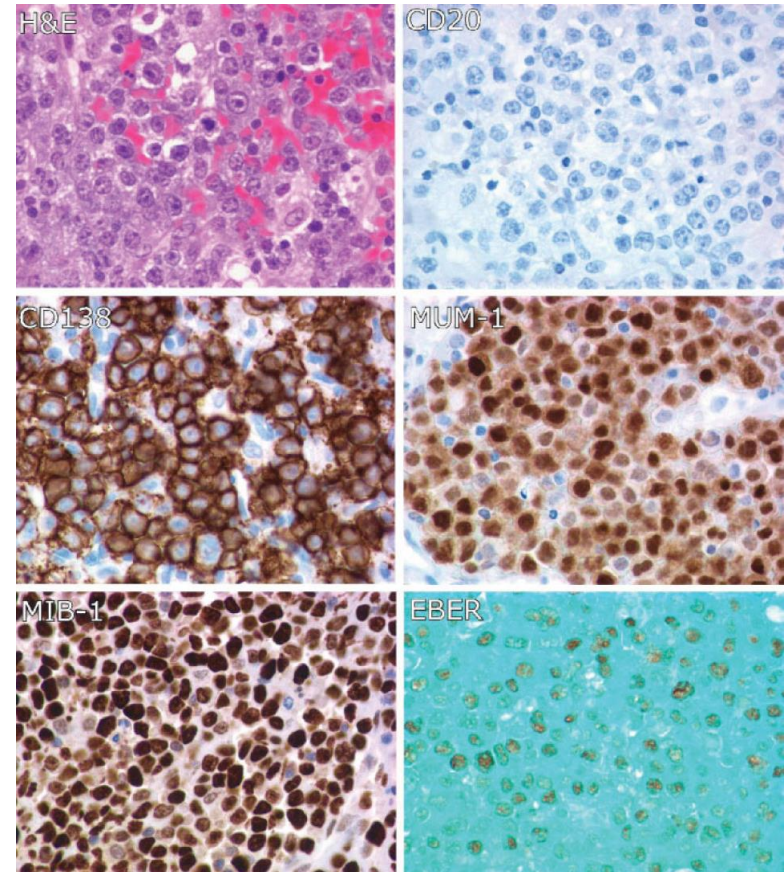
- N=16
- 14 men
- 15 HIV+
- 11 stage I; 5 stage IV
- 6 chemo; 4 RT; 6 chemo-RT
- 10 died
- 2 alive
- Median OS 6 months



**PBL is a real and distinct entity**

# HIV-associated plasmablastic lymphoma: Lessons learned from 112 published cases

	N	%
Age ( <i>n</i> = 112)		
Median (years)	38	
Range (years)	7–65	
Sex ( <i>n</i> = 107)		
Male	94	88
Female	13	12
CD4 count ( <i>n</i> = 28)		
Median (cells/mm <sup>3</sup> )	178	
Range (cells/mm <sup>3</sup> )	10–498	
Duration of HIV infection ( <i>n</i> = 18)		
Median (years)	5	
Range (years)	0–20	
Ann arbor stage ( <i>n</i> = 85)		
I	49	58
II	2	2
III	0	0
IV	34	40
Primary lymphoma site ( <i>n</i> = 112)		
Oral	65	58
Gastrointestinal tract	14	13
Lymph nodes	7	6
Other extranodal nonoral sites <sup>a</sup>	26	23
Therapy ( <i>n</i> = 53)		
CHOP alone	16	30
Other chemotherapy regimens	13	25
Chemoradiotherapy (including CHOP)	11	21
Other therapies <sup>b</sup>	7	13
No therapy	6	11

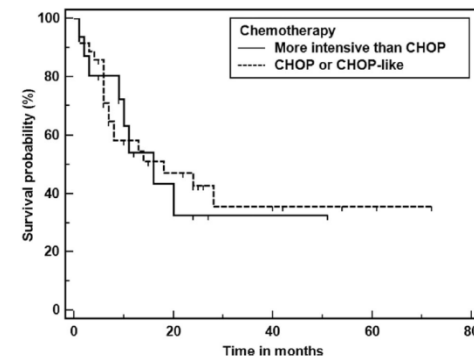
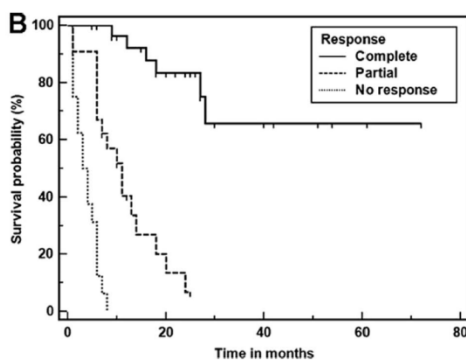
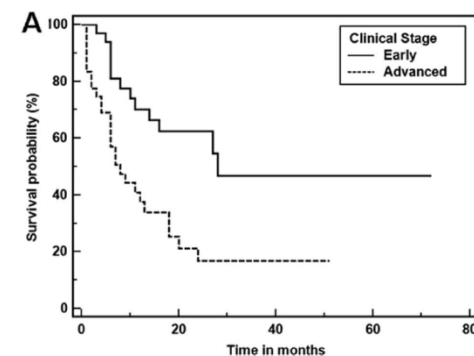
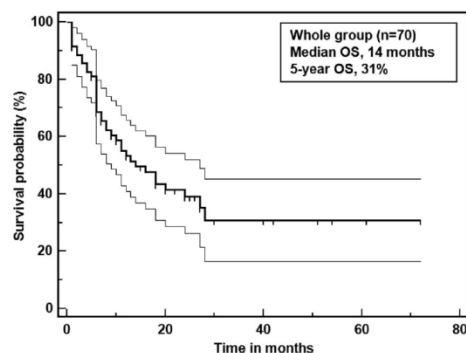


Castillo et al. Am J Hematol 2008

**There is PBL outside of the oral cavity**

# Prognostic Factors in Chemotherapy-Treated Patients with HIV-Associated Plasmablastic Lymphoma

Characteristic	<i>n</i>	Percentage
<b>Age (<i>n</i> = 70)</b>		
<40 yrs	28	40%
≥40 yrs	42	60%
<b>CD4<sup>+</sup> cell count (<i>n</i> = 29)</b>		
<200/mm <sup>3</sup>	18	62%
<100/mm <sup>3</sup>	13	45%
<50/mm <sup>3</sup>	11	38%
<b>Clinical stage (<i>n</i> = 70)</b>		
Early (1 or 2)	34	49%
Advanced (3 or 4)	36	51%
<b>Chemotherapy (<i>n</i> = 70)</b>		
CHOP or CHOP-like	35	50%
More intensive than CHOP	16	23%
Other regimen	19	27%
<b>Response to chemotherapy (<i>n</i> = 70)</b>		
Complete response	32	46%
Partial response	22	31%
No response	16	23%

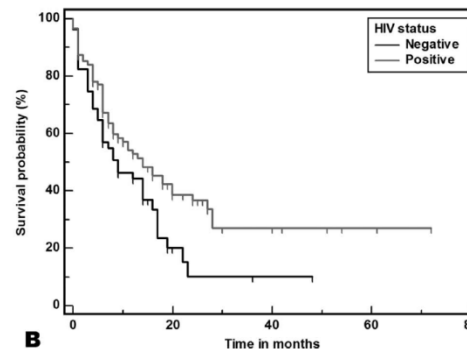


**Survival is short, regardless of treatment**

# Clinical and pathological differences between human immunodeficiency virus-positive and human immunodeficiency virus-negative patients with plasmablastic lymphoma

	HIV-positive	HIV-negative
Total	157 (69%)	71 (31%)
Age ( <i>n</i> = 223)		
Older than 60 years	2 (1%)	33 (47%)
60 years or younger	151 (99%)	37 (53%)
Mean age (range)	39 (3–65)	58 (1–90)
Sex ( <i>n</i> = 228)		
Male	128 (82%)	44 (62%)
Female	29 (18%)	27 (38%)
Stage ( <i>n</i> = 174)		
I	42 (37%)	14 (23%)
II	13 (12%)	10 (16%)
III	1 (1%)	9 (15%)
IV	57 (50%)	28 (46%)
Site of involvement ( <i>n</i> = 213)		
Oral	88 (58%)	10 (16%)
Extraoral	64 (42%)	51 (84%)
Bone marrow ( <i>n</i> = 83)		
Involved	17 (30%)	8 (30%)
Not involved	39 (70%)	19 (70%)
B symptoms ( <i>n</i> = 69)		
Present	15 (33%)	13 (54%)
Absent	30 (67%)	11 (46%)
Therapy ( <i>n</i> = 120)		
Chemotherapy	59 (77%)	35 (81%)
No chemotherapy	18 (23%)	8 (19%)
Response to therapy ( <i>n</i> = 78)		
Complete response	23 (55%)	15 (42%)
Partial response	11 (26%)	5 (14%)
Stable disease	0 (0%)	6 (16%)
Progressive disease	8 (19%)	10 (28%)

	HIV-positive	HIV-negative
CD45 expression ( <i>n</i> = 136)		
Positive	56 (50%)	17 (68%)
Negative	55 (50%)	8 (32%)
CD20 expression ( <i>n</i> = 156)		
Positive	21 (17%)	0 (0%)
Negative	99 (83%)	36 (100%)
CD79a expression ( <i>n</i> = 93)		
Positive	31 (51%)	12 (37%)
Negative	30 (49%)	20 (63%)
CD4 expression ( <i>n</i> = 12)		
Positive	2 (22%)	1 (33%)
Negative	7 (78%)	2 (67%)
CD56 expression ( <i>n</i> = 38)		
Positive	14 (67%)	1 (6%)
Negative	7 (33%)	16 (94%)
BCL-2 expression ( <i>n</i> = 31)		
Positive	4 (17%)	2 (25%)
Negative	19 (83%)	6 (75%)
Ki-67 expression ( <i>n</i> = 73)		
80% or higher	39 (75%)	13 (62%)
Lower than 80%	13 (25%)	8 (38%)
EBER expression ( <i>n</i> = 142)		
Positive	83 (82%)	19 (46%)
Negative	18 (18%)	22 (54%)



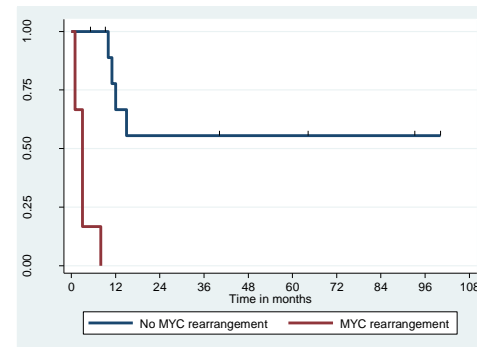
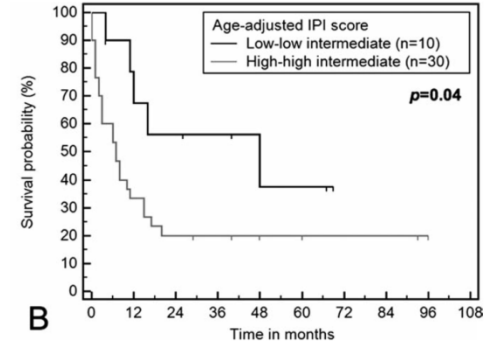
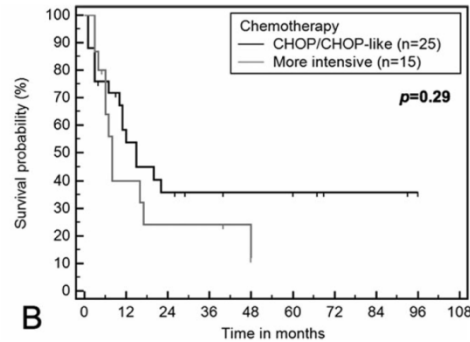
**There is PBL in HIV-negative patients and it might have a worse survival**

# Human Immunodeficiency Virus-Associated Plasmablastic Lymphoma

Poor Prognosis in the Era of Highly Active Antiretroviral Therapy

## Patients' characteristics

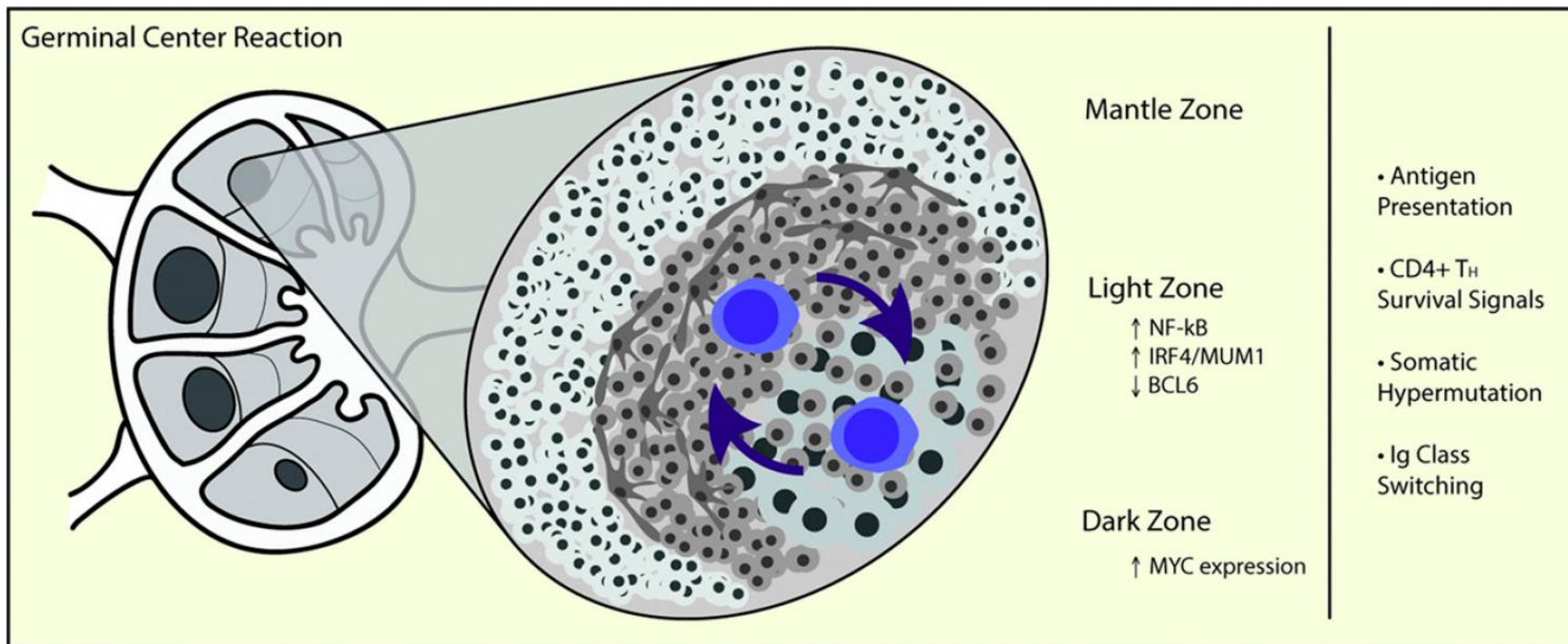
- N=50
- Men 78%
- CD4+ count >200 42%
- HAART 100%
- Stage III/IV 69%
- CHOP 63%
- Other 37%
- *MYC* rearrangement 41%
- ALK 0%
- HHV8 LANA/PCR 0%



**Even with chemotherapy and HAART, PBL patients have a bad outcome**

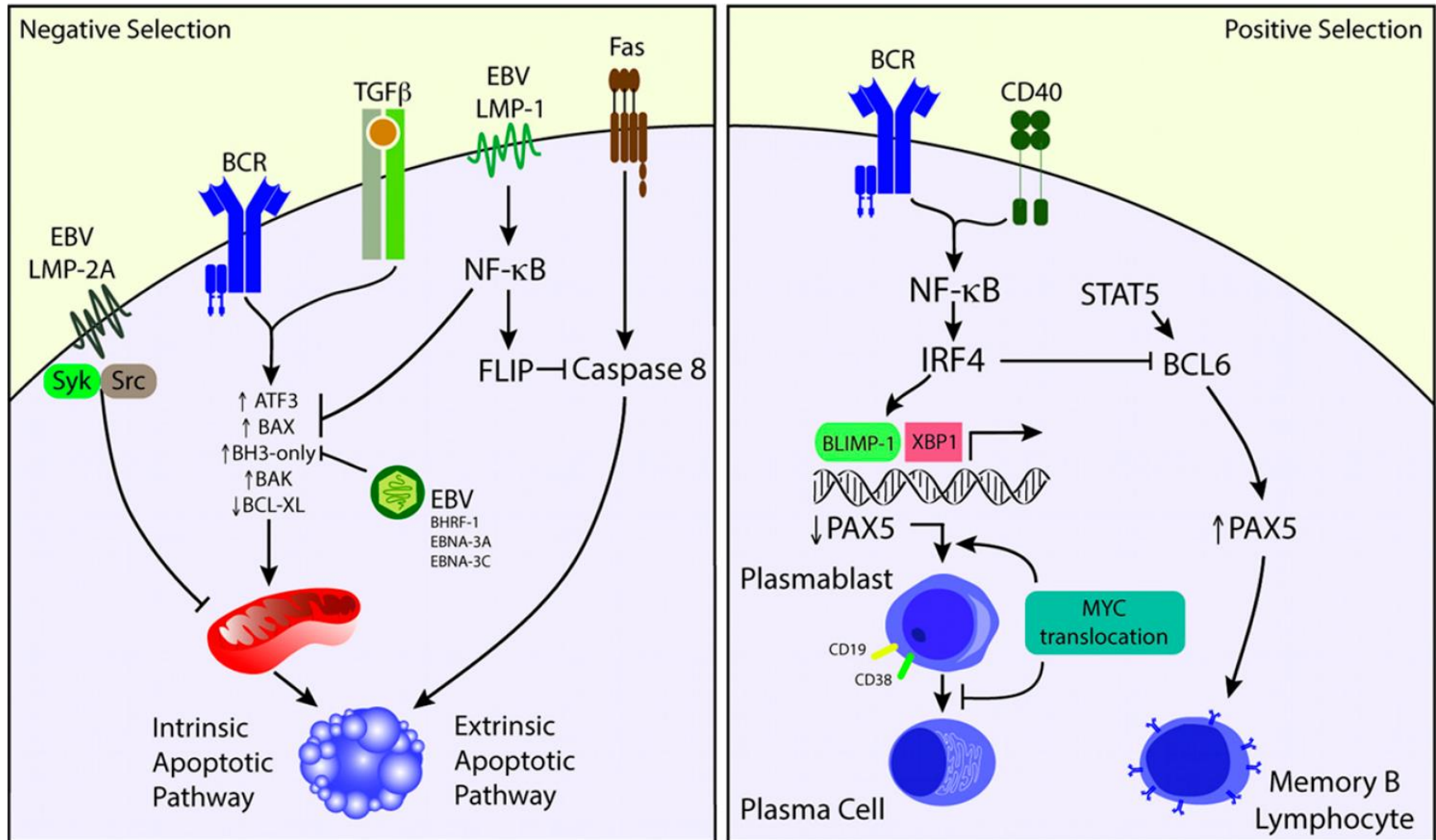
Castillo et al. Cancer 2012

# The biology and treatment of plasmablastic lymphoma



Castillo et al. Blood 2015

# The biology and treatment of plasmablastic lymphoma

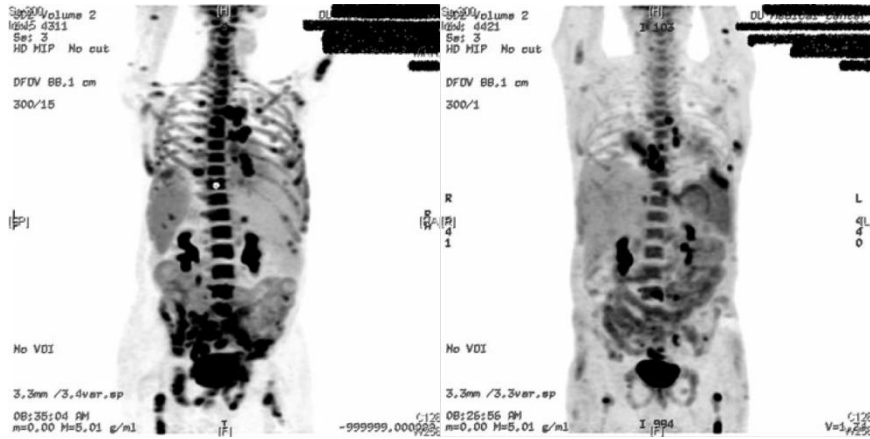


Castillo et al. Blood 2015

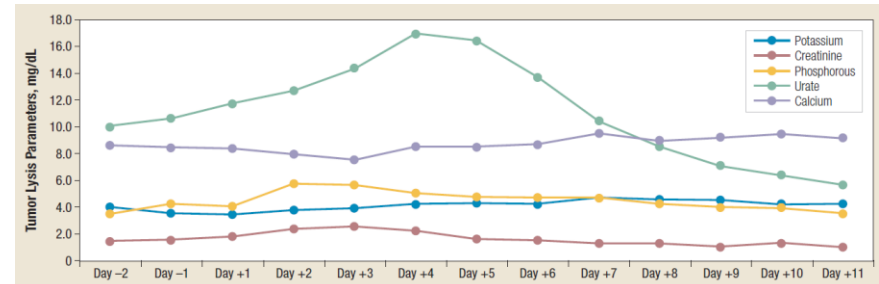


# Reports on bortezomib in PBL

## AIDS-related plasmablastic lymphoma with dramatic, early response to bortezomib

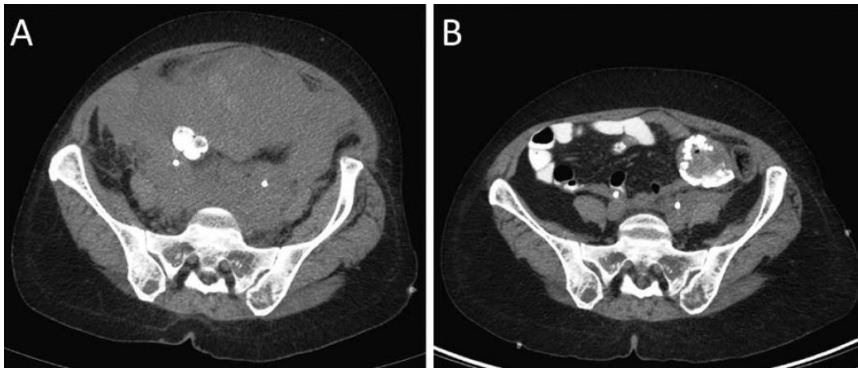


## Bortezomib-Induced Tumor Lysis Syndrome in a Patient With HIV-Negative Plasmablastic Lymphoma



A striking response of plasmablastic lymphoma of the oral cavity to bortezomib:

## Bortezomib in Plasmablastic Lymphoma: A Case Report and Review of the Literature



Bose. Eur J Haematol 2009; Lipstein. Clin Lymphoma Leuk Myeloma 2010; Saba. Onkologie 2013; Hiroswa. Biomarker Res 2015

# Bortezomib in combination with infusional dose-adjusted EPOCH for the treatment of plasmablastic lymphoma

## Patients

### Case 1

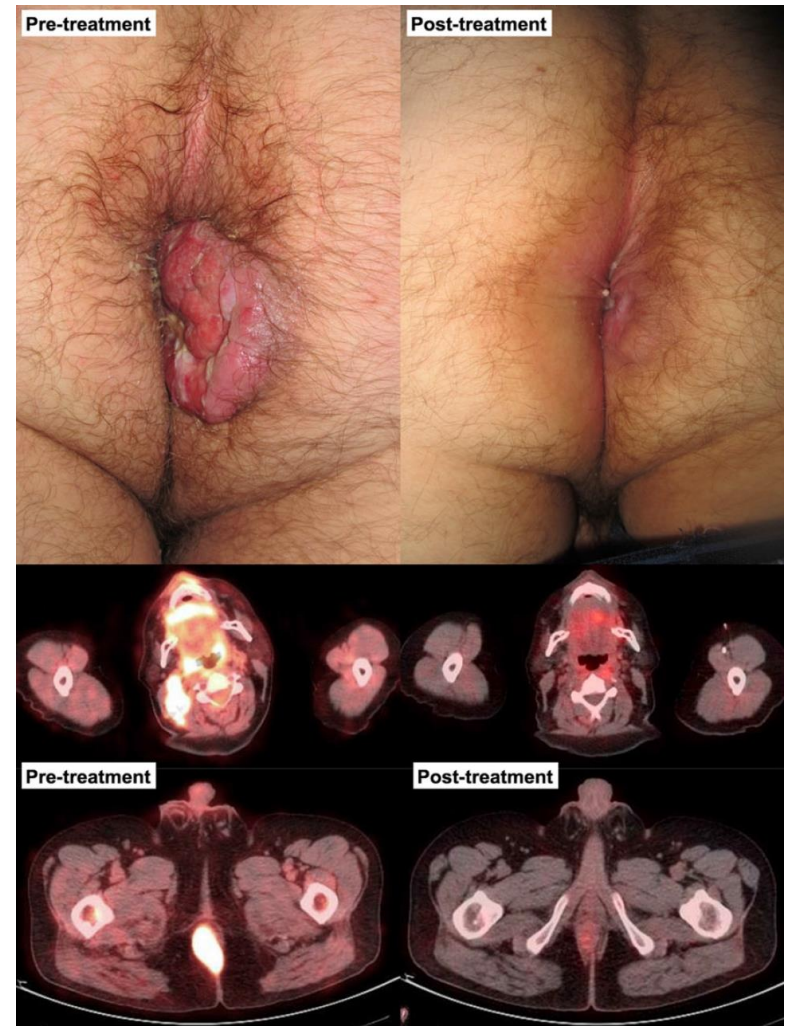
- 40M, HIV+, CD4 290, stage IV (rectal and pharyngeal), MYC+ 60%, EBER+, alive at 4 years

### Case 2

- 36M, HIV+, CD4 34, stage IV (rectal and lung nodules), EBER+, alive at 3 years

### Case 3

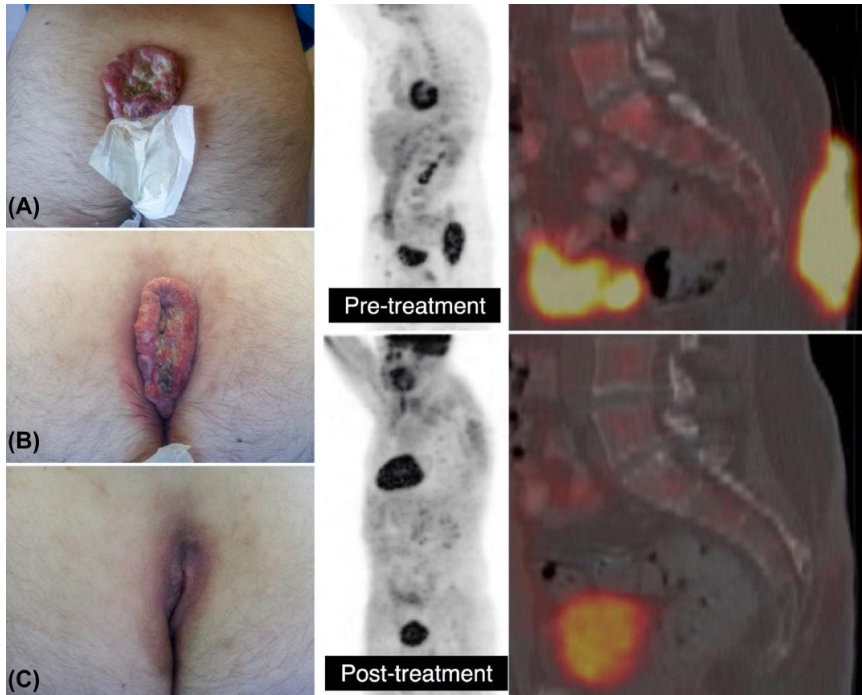
- 66M, HIV-, stage II (non-obstructing colonic mass), MYC+ 15%, alive at 2.5 years



Castillo et al. Br J Haematol 2015

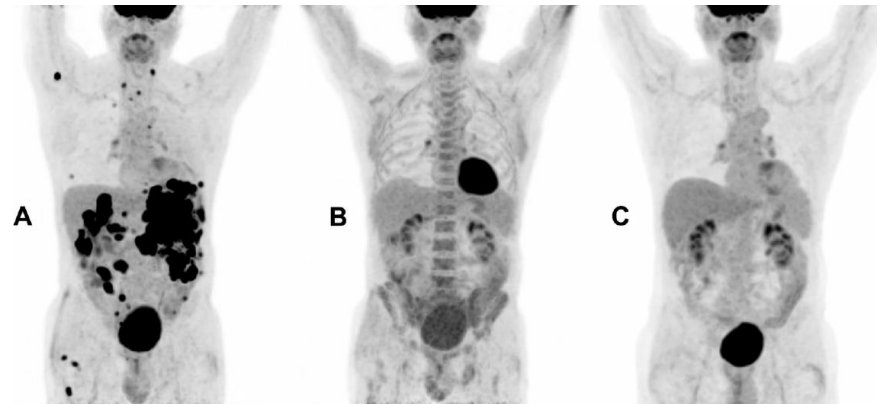
# Reports on bortezomib and chemotherapy in PBL

Bortezomib plus CHOP for the treatment of HIV-associated plasmablastic lymphoma: clinical experience in three patients



2 patients alive at 12 and 24 months;  
1 patient died at 12 months

Infusional dose-adjusted epoch plus bortezomib for the treatment of plasmablastic lymphoma



Patient alive at 2 years

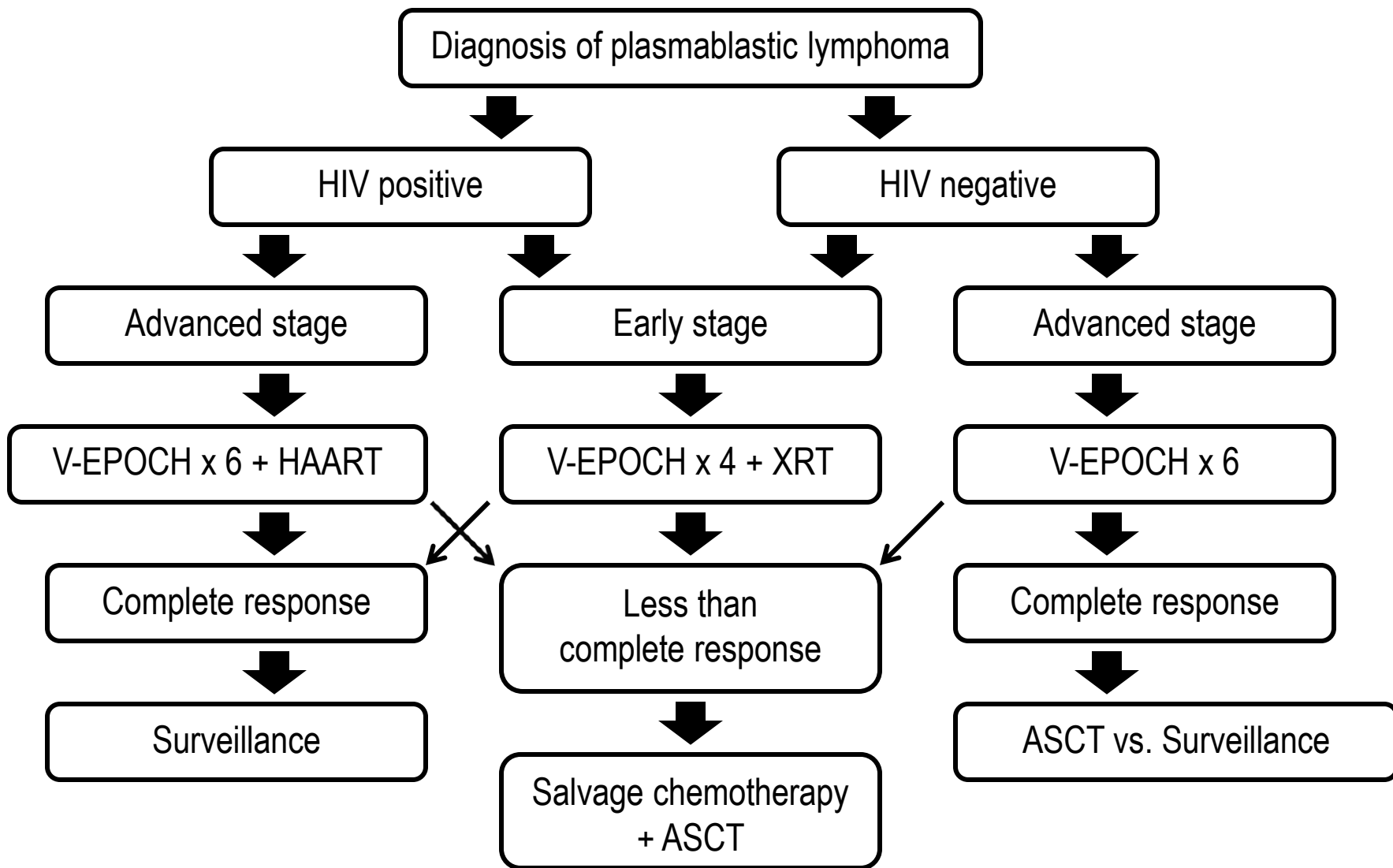
Fernandez-Alvarez et al. Leuk Lymphoma 2016  
Fedele et al. Ann Hematol 2016

# The role of transplant in PBL

Case Reports of HIV-Negative Patients with PBL and Their Reported Outcome in Literature

Patient No. [Ref]	Age, yr	Gender (M/F)	Stage	Immune Status	aaIPI	Induction Regimen	Disease Status before AHCT	Conditioning Regimen	Disease Status after AHCT	DFS after AHCT, mo	OS at Last follow-up, mo
1 [18,21]	23	M	IV	Competent	2	HyperCVAD × 2 PD: IVAC × 3	PR2	BEAM	CR	5	12 (died)
2 [18,75]	57	M	IV	Cardiac transplant (cyclosporine)	2	Cyclosporine w/d Cy/MTX PD: ICE × 3	PR2	Chemo-based	PD	PD	6 (died)
3 [18]	63	F	IV	Competent	5	HyperCVAD × 4	CR1	BEAM	CR	2	13.3 (died)
4 [18]	60	F	IV	Competent	3	HyperCVAD × 4	PR1	BEAM	CR	14	36.5 (died)
5 [18]	64	M	IIE	Competent	2	R-CHOP × 6	CR1	BEAM	CR	A-NED	25.3
6 [18]	67	M	IV	Competent	3	CHOP × 1 R-CHOP × 5	CR1	BEAM	CR	A-NED	46.7
7 [60]	36	M	IV	Competent	2	ProMACE/CytaBOM	CR1	BEAM	CR	NR	16.9 (died)
8 [60]	52	F	II	Competent	1	CHOP × 6 PD: MiniBEAM	PR2	Cy-TBI	CR	2.5	17.2 (died)
9 [60]	50	M	II	Competent	0	CHOP: RD MiniBEAM: RD ICE	RD/CR1	BEAM	PD	PD	14 (died)

# Recommended treatment algorithm



# Key messages

- PBL is a real and distinct entity
- There is PBL outside of the oral cavity
- There is PBL in HIV-negative patients and it might have a worse survival
- Survival is short, regardless of treatment
- Bortezomib in combination with chemotherapy might improve outcomes in PBL
- ASCT in CR1 might improve outcomes in HIV-negative PBL

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