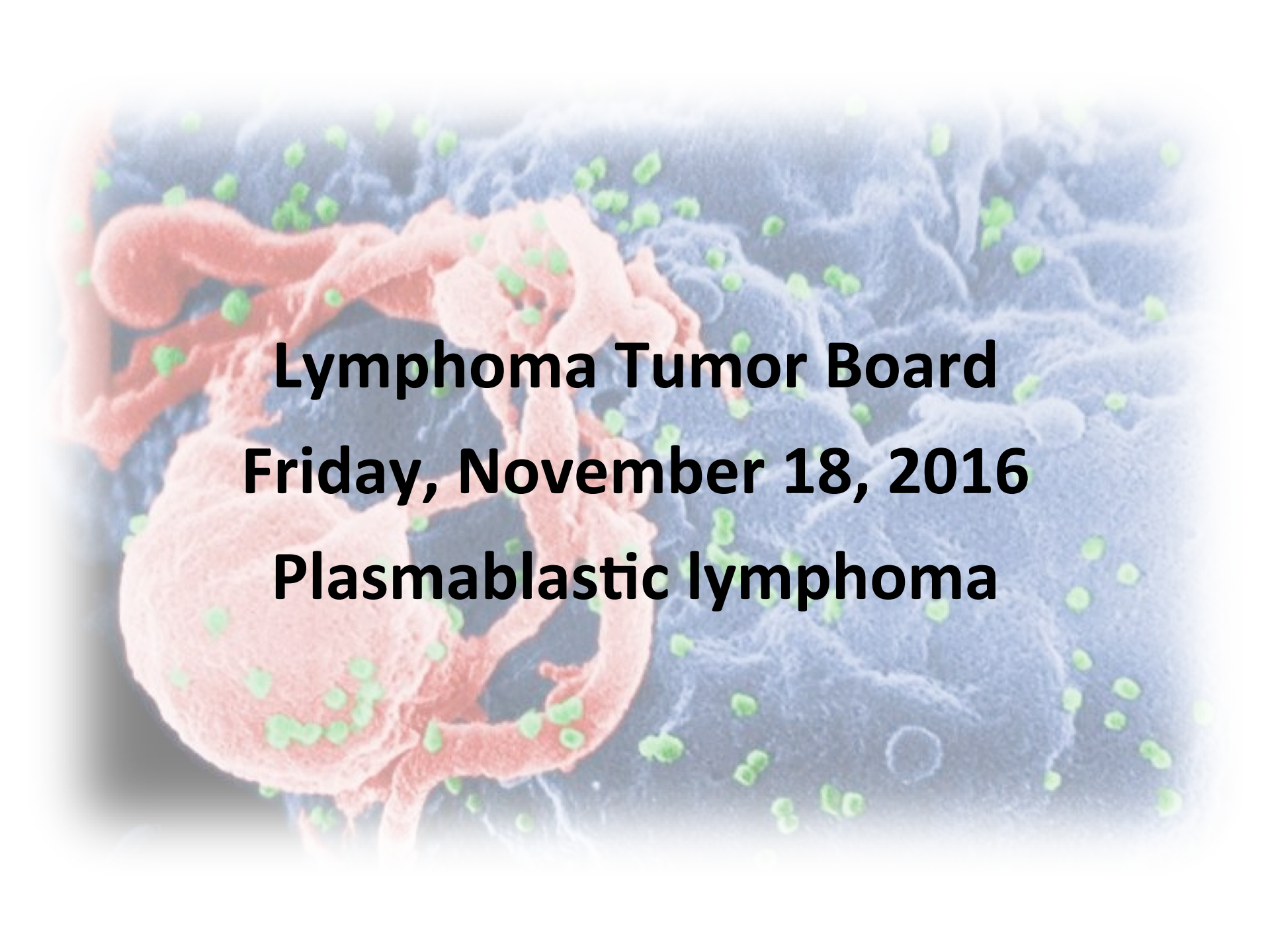


Lymphoma Tumor Board

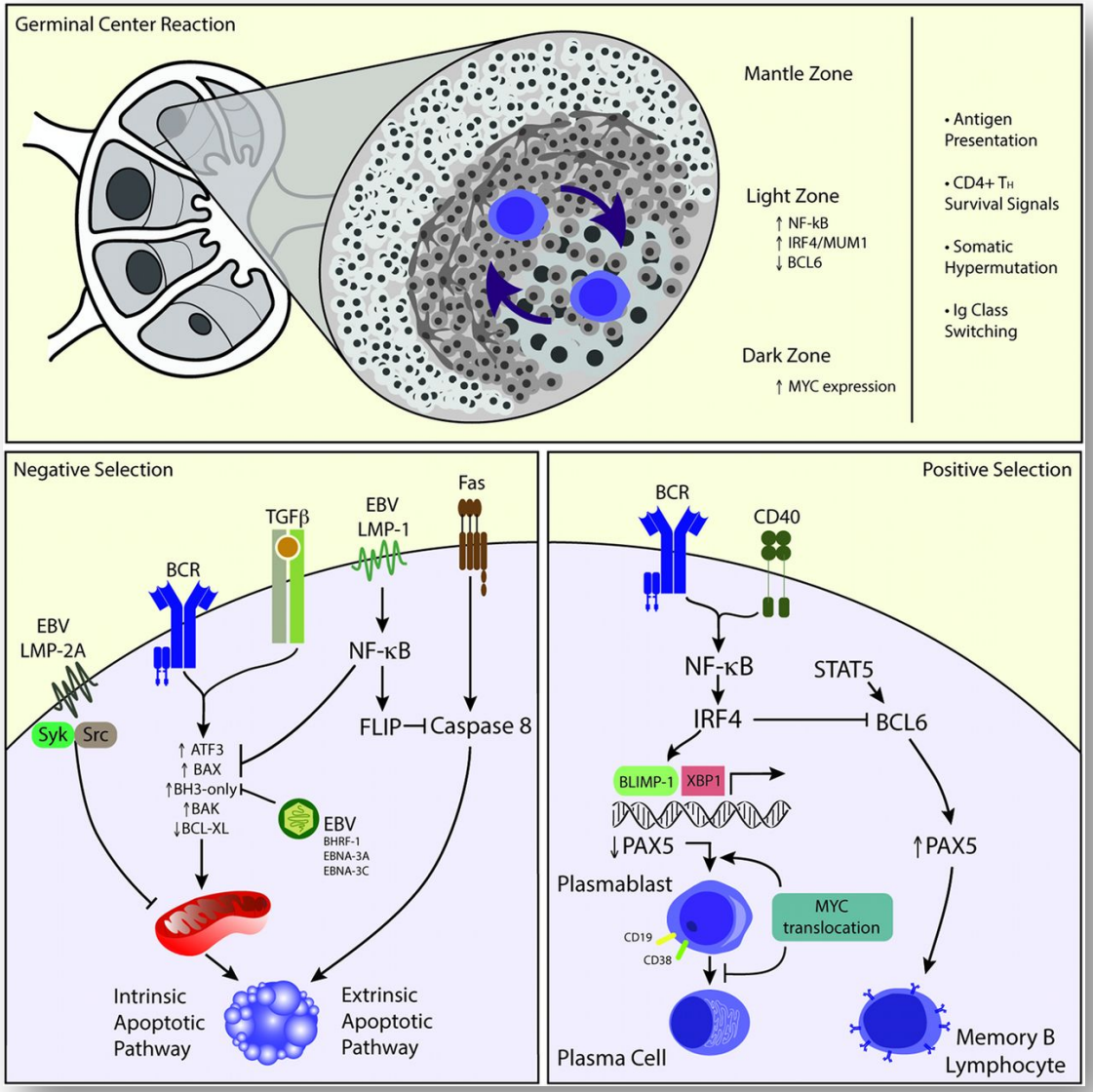
Friday, November 18, 2016

Plasmablastic lymphoma

Plasmablastic lymphoma - Background

- Aggressive lymphoma associated with HIV infection and other conditions associated with immune deficiency
- B-cell lineage, but CD20-negative
- Immunophenotype of tumor cells generally resembles that of plasma cells
- Median age at diagnosis is 40-60
- Predilection for the oral cavity, nasal cavity, gastrointestinal tract, skin, bone soft tissue, and lung
- Morphology resembles that of Burkitt lymphoma with a "starry sky" appearance
  - HHV-8 (KSHV) typically not detected
  - EBV positive in 75%

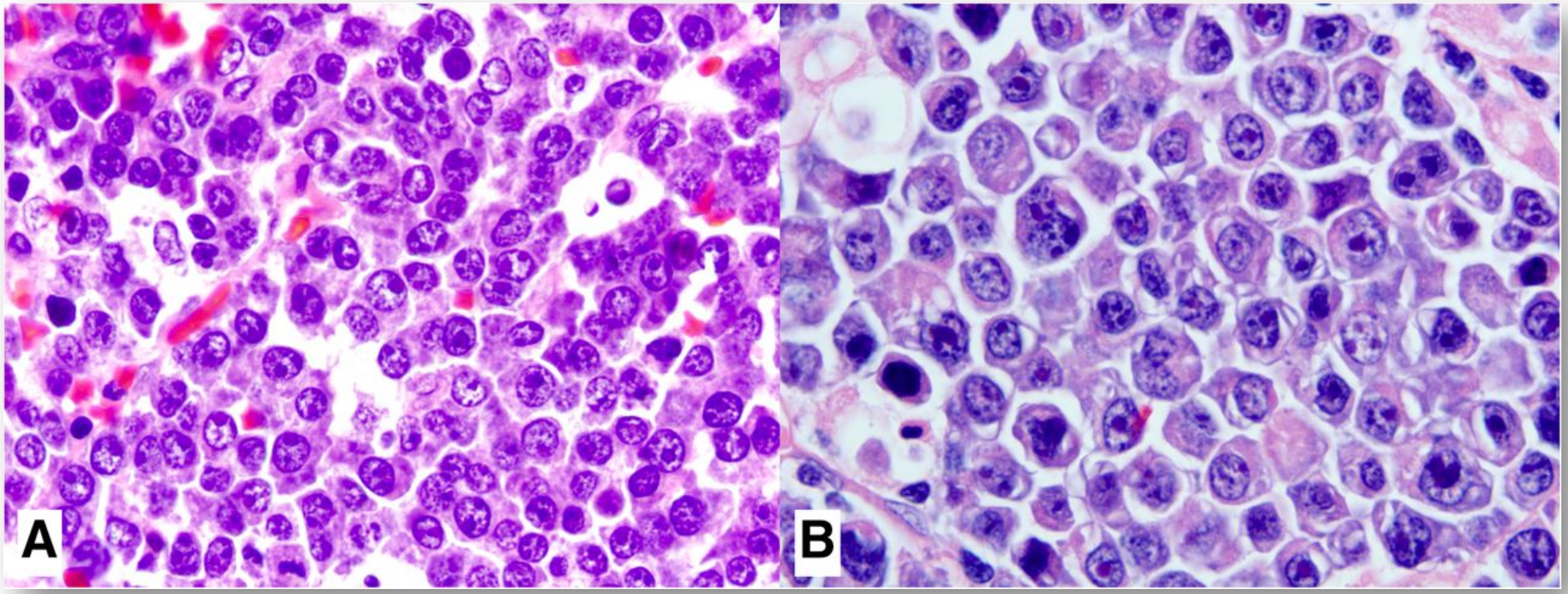
PBL biology : GC reaction in primary follicle



Jorge J. Castillo et al. Blood 2015;125:2323-2330

blood

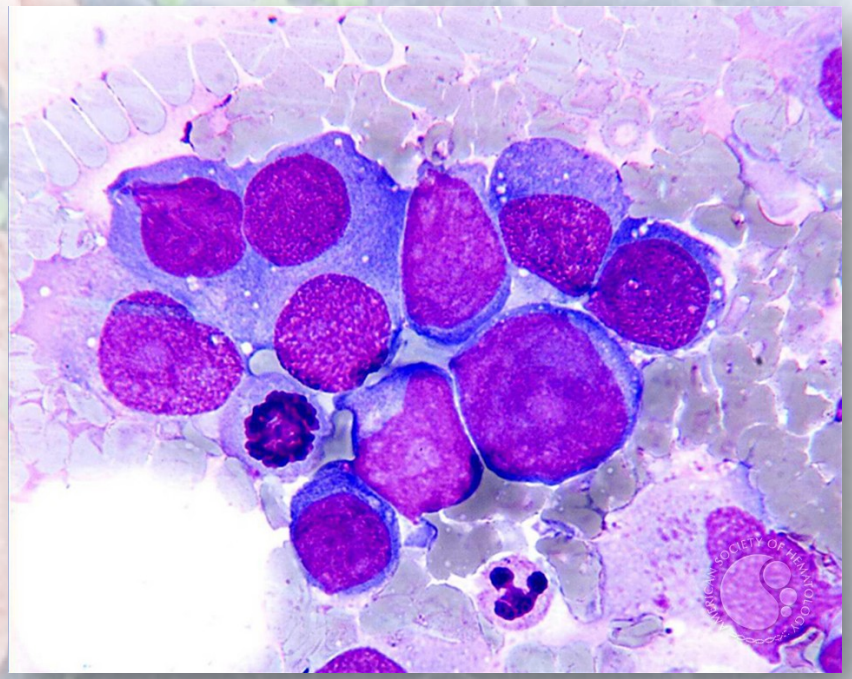
PBL: Histopathologic features in HIV^{+} setting



Jorge J. Castillo et al. Blood 2015;125:2323-2330

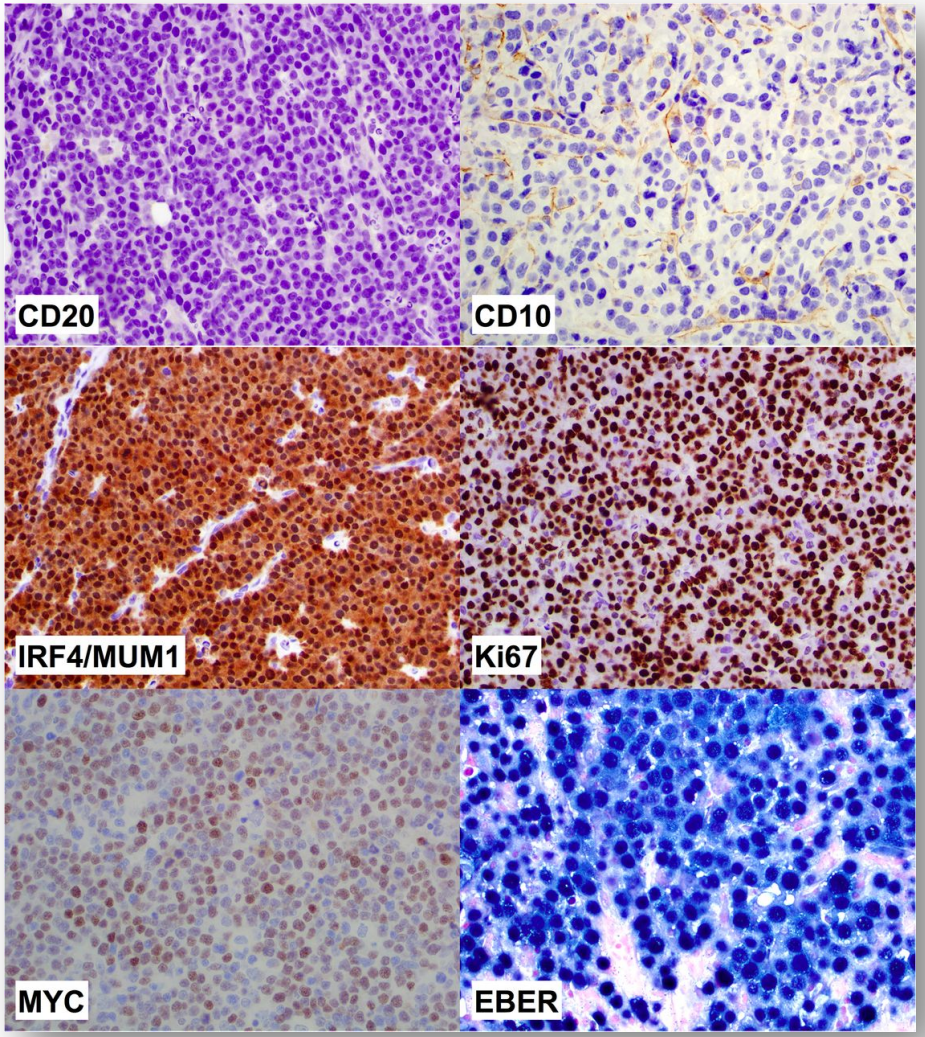
Immunophenotype of plasmablastic lymphoma

- Viewed as clinicopathologic variant of DLBCL
- Castillo *et al*. studied phenotypic variability within PBL to identify a specific IHC profile that would reliably distinguish it from DLBCL
- Markers studied:
  - CD20
  - PAX5
  - BCL6
  - CD10
  - GCET1
  - KLHL6
  - IRF4/MUM1
  - PRDM1/BLIMP1
  - XBP1
  - CD38
  - CD138
  - Ki-67(MIB-1)
  - p53
  - ISH for EBV EBER
- Plasmablastic lymphoma comprises two primary immunophenotypes



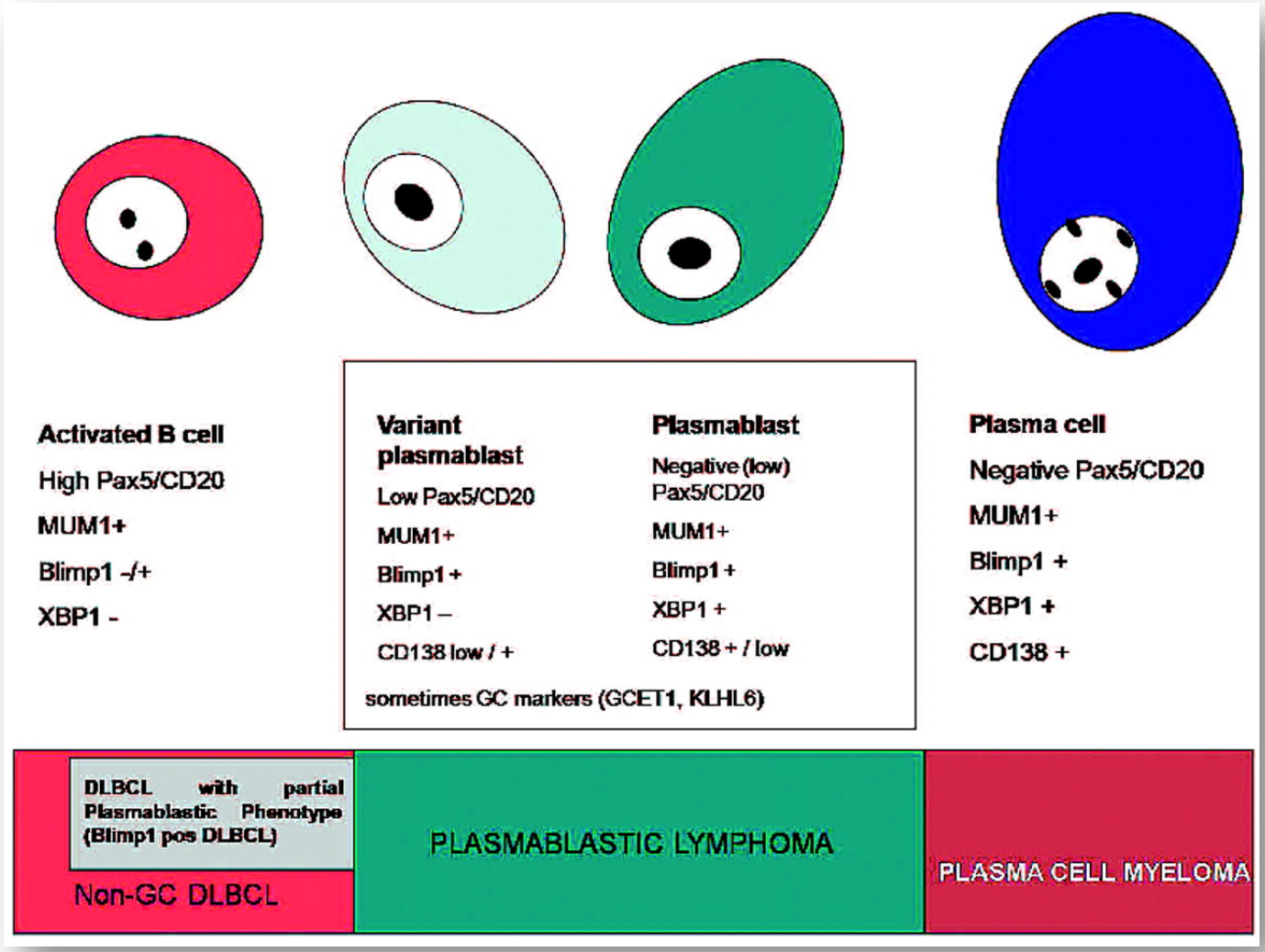
ASH | Image Bank

PBL immunophenotype: lack of expression of CD10 and CD20; reliable expression of IRF4/MUM1 and MYC; high Ki-67



Jorge J. Castillo et al. Blood 2015;125:2323-2330

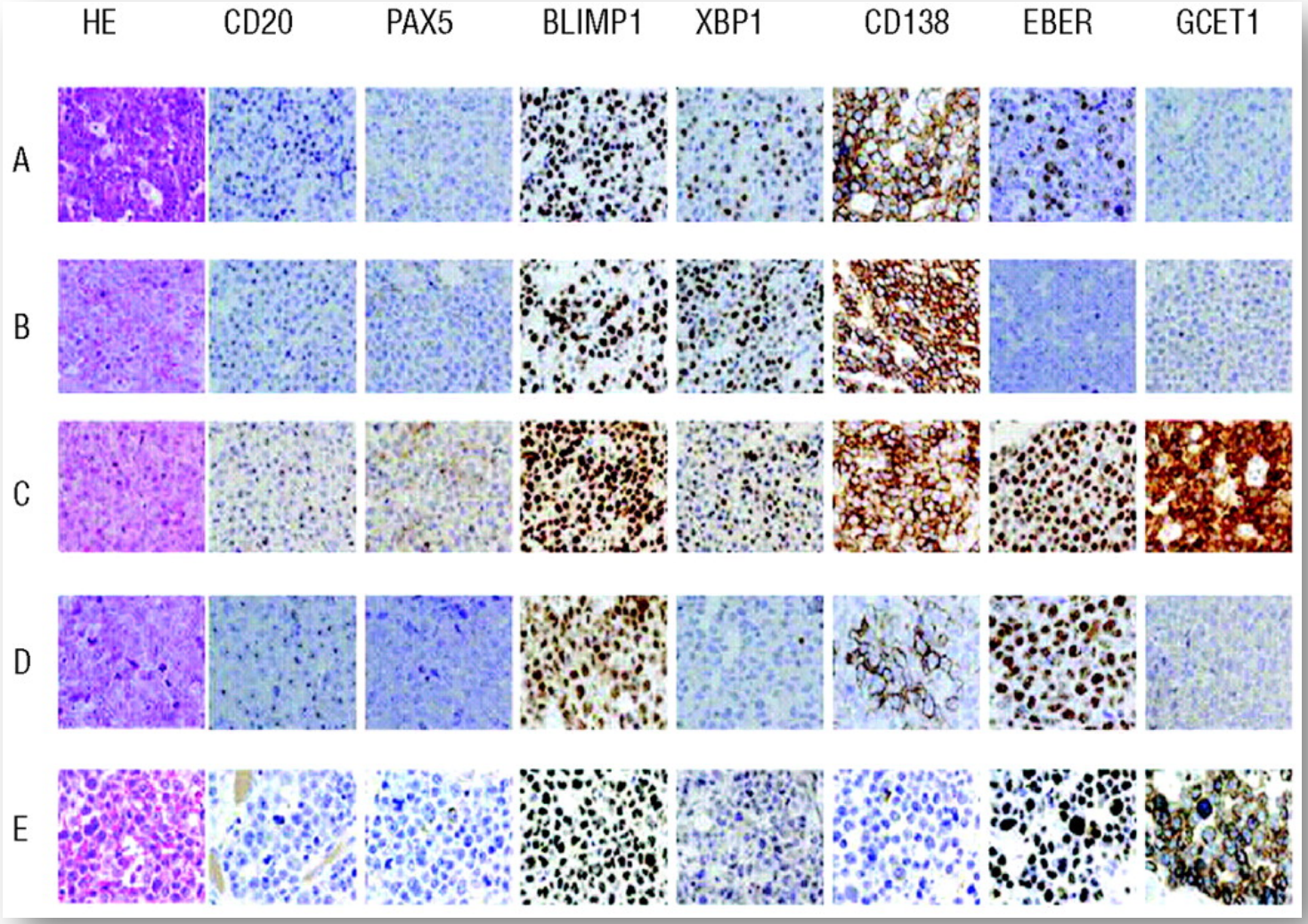
Expression of PAX5, CD20, PRDM1/BLIMP1, XBP1 characterizes the immunophenotype of plasmablastic lymphoma



Santiago Montes-Moreno et al. Haematologica 2010;95:1342-1349

haematologica
Journal of the European Hematology Association
Published by the Ferrata Storti Foundation

Phenotypic heterogeneity in plasmablastic lymphoma



Santiago Montes-Moreno et al. Haematologica 2010;95:1342-1349

haematologica
Journal of the European Hematology Association
Published by the Ferrata Storti Foundation

Differential diagnosis of PBL and related lymphomas

Table 3. Differential diagnosis of PBL

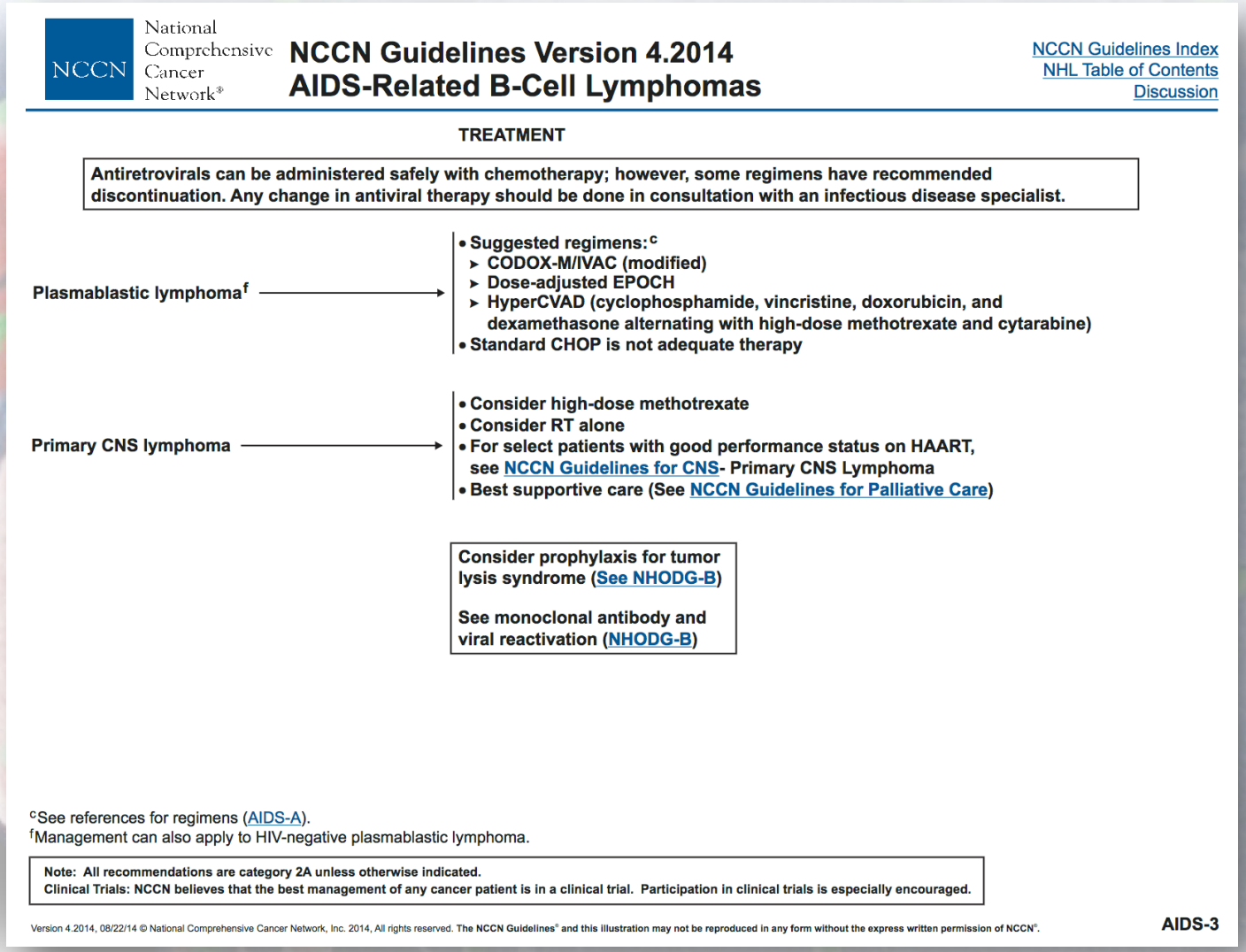
	PBL	Plasmablastic myeloma	LBCL HHV-8–positive	IBL DLBLC	ALK-positive DLBCL	DLBCL ACI	PEL
Disease distribution	Extranodal	Bone marrow and extranodal	Nodal	Nodal	Nodal	Extranodal	Extranodal
HIV infection	~70%	No	Yes	No	No	No	Yes
Pathogenesis	EBV, HIV, IL-10	IL-6	HHV-8, MCD		ALK	EBV, IL-10, IL-6	HHV-8
Positive markers	CD138, IRF-4/MUM-1, MYC	CD138, cytoplasmic Ig, MYC	$CD20^{-/+}$, $CD138^{+/-}$, IgM	CD20, PAX-5,	ALK, CD4, CD45	CD20, CD4	IRF-4/MUM-1, $CD30^{-/+}$
Negative markers	CD20, PAX-5	CD20, PAX-5, BCL-6	CD138	CD4, CD138	CD20, CD30, MYC	ALK	PAX-5, CD20, CD138, Ig
Proliferation rate	>90%	>90%	>90%	~80%	>90%	>90%	>90%
Cytoplasmic immunoglobulin	50%-70%	>90%	IgA λ	Uncommon	Uncommon	Uncommon	Uncommon
EBV infection	Common	No	No	No	No	Common	Common
EBV latency pattern	I	NA	NA	NA	NA	III	I
HHV-8 infection	No	No	Yes	No	No	No	Yes
Molecular genetics	MYC GR	Myeloma FISH abnormalities	Unmutated Ig	MYC GR	t(2;17)(p23;q23)	TP53 mutations	Hypermutated Is

ACI, associated with chronic inflammation; ALK, anaplastic lymphoma kinase; FISH, fluorescence in situ hybridization; GR, gene rearrangement; IBL, immunoblastic; IL, interleukin; IRF-4/MUM-1, interferon regulatory factor 4/multiple myeloma 1; LBCL, large B-cell lymphoma; NA, not available; PEL, primary effusion lymphoma.

Treatment of plasmablastic lymphoma

- Prognosis is generally poor
- *MYC* rearrangements have been shown to be associated with shorter OS
- CHOP, infusional EPOCH, hyperCVAD, and CODOX-M/IVAC are mainstays of therapy
- Intrathecal prophylaxis should be considered
- In the US, "first-line treatment of PBL is 6 cycles of infusional dose-adjusted EPOCH (with or without bortezomib) with intrathecal prophylaxis with each cycle of EPOCH and consideration of consolidative HDC followed by autologous SCT in first remission for appropriate candidates."
- HIV^+ individuals should be started on cART and optimized to ensure there are no interactions between anticancer agents and cART

Treatment of plasmablastic lymphoma - NCCN



National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2014
AIDS-Related B-Cell Lymphomas

NCCN Guidelines Index
NHL Table of Contents
Discussion

TREATMENT

Antiretrovirals can be administered safely with chemotherapy; however, some regimens have recommended discontinuation. Any change in antiviral therapy should be done in consultation with an infectious disease specialist.

Plasmablastic lymphoma[f] →
- **Suggested regimens:[c]**
  - **CODOX-M/IVAC (modified)**
  - **Dose-adjusted EPOCH**
  - **HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine)**
- **Standard CHOP is not adequate therapy**

Primary CNS lymphoma →
- **Consider high-dose methotrexate**
- **Consider RT alone**
- **For select patients with good performance status on HAART, see NCCN Guidelines for CNS- Primary CNS Lymphoma**
- **Best supportive care (See NCCN Guidelines for Palliative Care)**

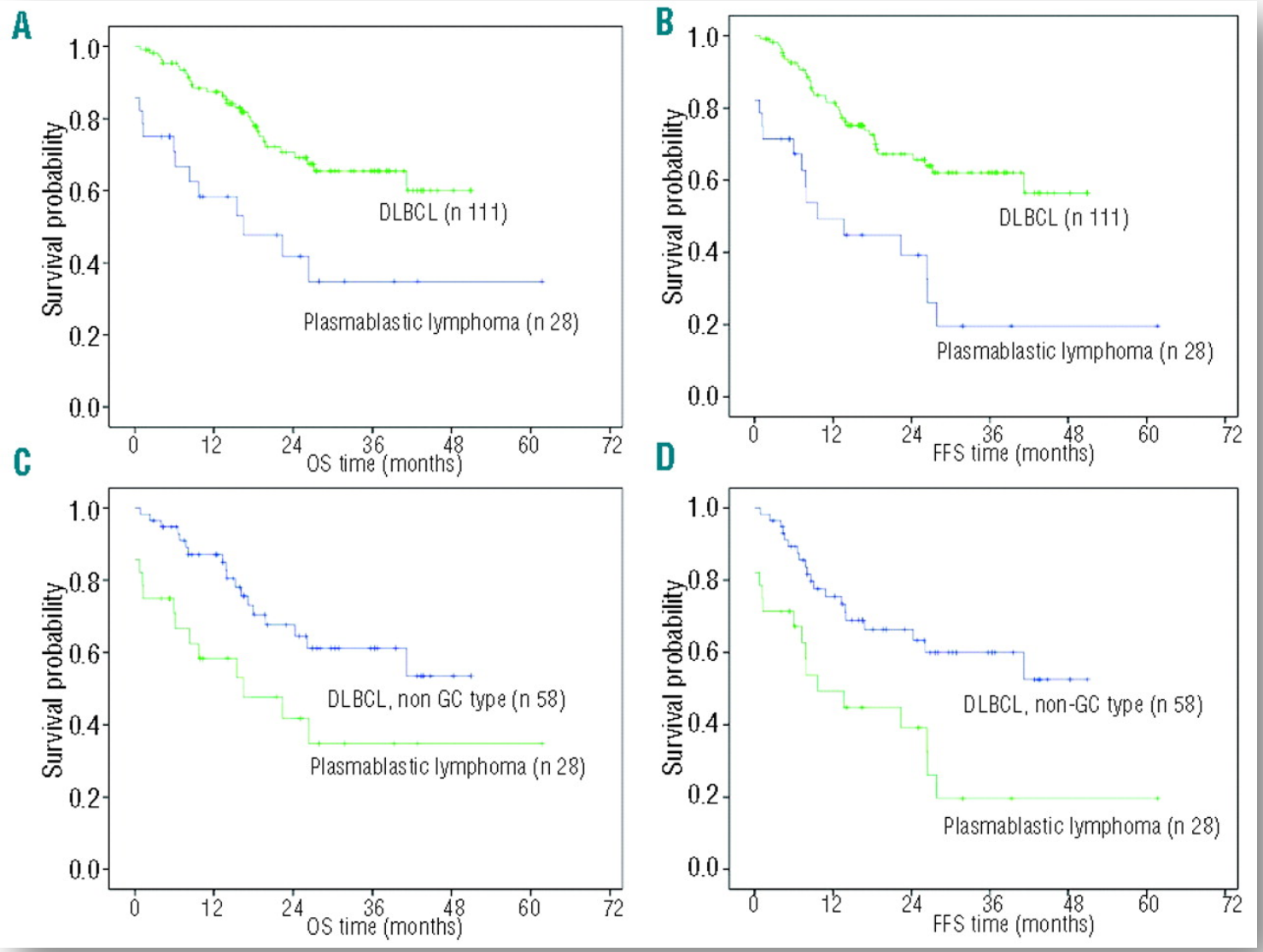
Consider prophylaxis for tumor lysis syndrome (See NHODG-B)

See monoclonal antibody and viral reactivation (NHODG-B)

[c]See references for regimens (AIDS-A).
[f]Management can also apply to HIV-negative plasmablastic lymphoma.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

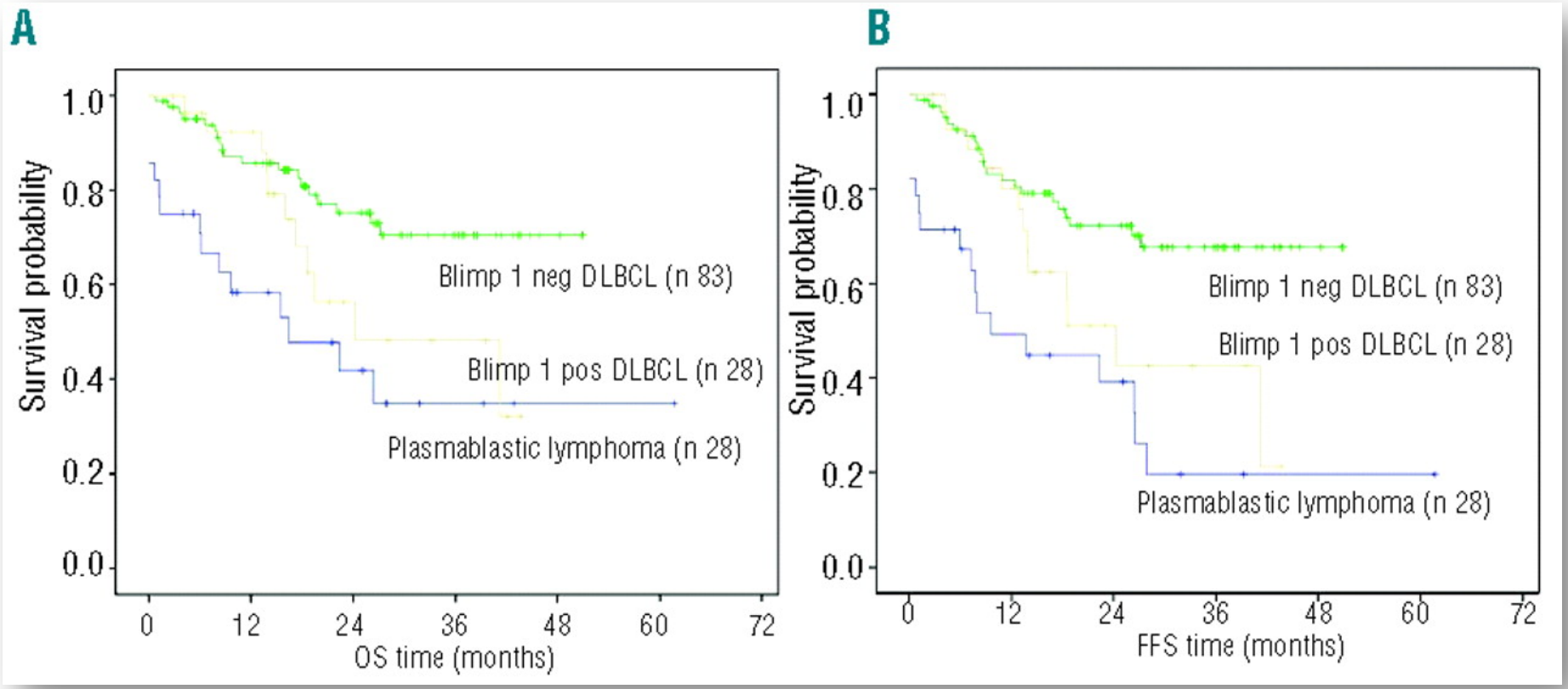
Survival in plasmablastic lymphoma vs. DLBCL



Santiago Montes-Moreno et al. Haematologica 2010;95:1342-1349

haematologica
Journal of the European Hematology Association
Published by the Ferrata Storti Foundation

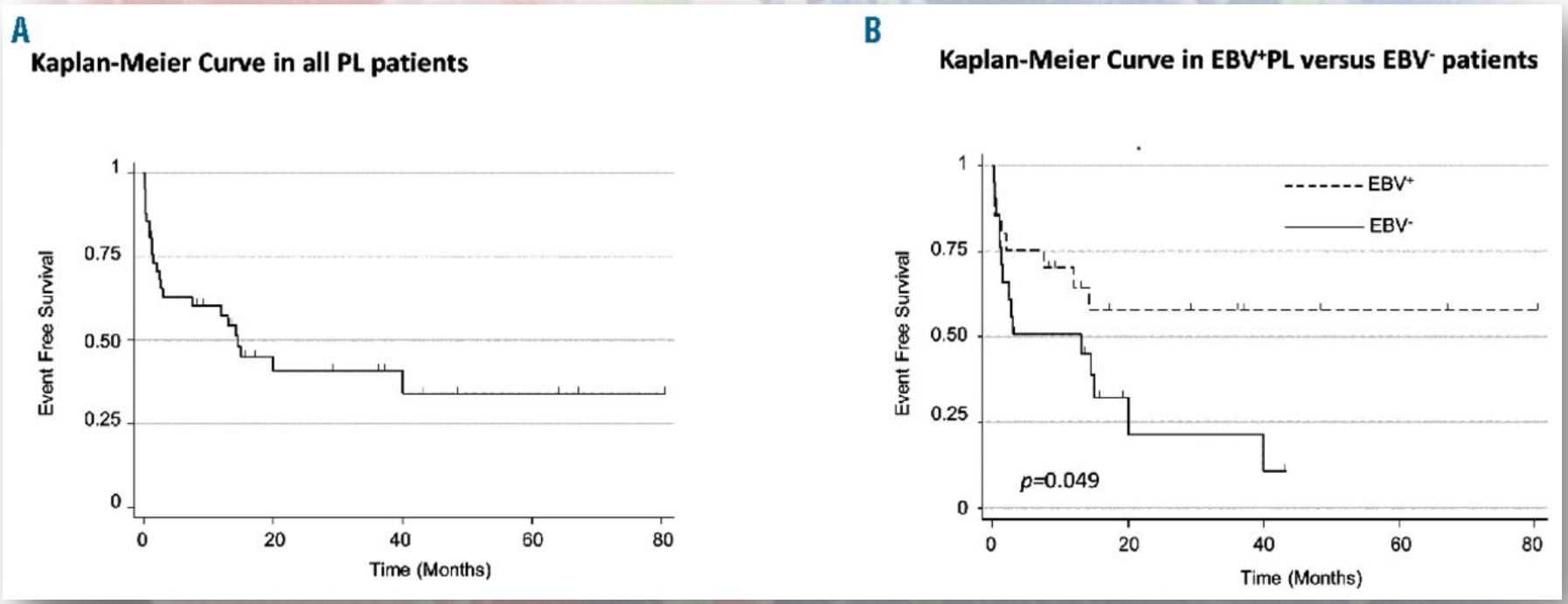
Significance of PRDM1/BLIMP1 expression in DLBCL and plasmablastic lymphoma



Santiago Montes-Moreno et al. Haematologica 2010;95:1342-1349

haematologica
Journal of the European Hematology Association
Published by the Ferrata Storti Foundation

Significance of EBV in plasmablastic lymphoma



Camille Laurent et al. Haematologica 2016;101:976-984

haematologica
Journal of the European Hematology Association
Published by the Ferrata Storti Foundation

Summary – Plasmablastic lymphoma

- Uncommon subtype of B-cell lymphoma
- No well-recognized standard of care
- Poor prognosis
- Intrathecal agents should be used to minimize the risk of CNS involvement/relapse
- New immunohistochemical profiles have been studied for better characterization of plasmablastic lymphoma
- Chemotherapy with CHOP, infusional EPOCH, hyperCVAD, and CODOX-M/IVAC are commonly used for treatment at this time
- Current treatment is inadequate and better regimens are needed

References

- Castillo, J. J., Bibas, M., & Miranda, R. N. (2015). The biology and treatment of plasmablastic lymphoma. Blood, (), blood-2014-10-567479. Accessed November 14, 2016. http://dx.doi.org/10.1182/blood-2014-10-567479.

- Montes-Moreno, S., Gonzalez-Medina, A.-R., Rodriguez-Pinilla, S.-M., Maestre, L., Sanchez-Verde, L., Roncador, G., … Piris, M. A. (2010). Aggressive large B-cell lymphoma with plasma cell differentiation: immunohistochemical characterization of plasmablastic lymphoma and diffuse large B-cell lymphoma with partial plasmablastic phenotype. *Haematologica*, *95*(8), 1342–1349. http://doi.org/10.3324/haematol.2009.016113

- Laurent, C., Fabiani, B., Do, C., Tchernonog, E., Cartron, G., Gravelle, P., … Coppo, P. (2016). Immune-checkpoint expression in Epstein-Barr virus positive and negative plasmablastic lymphoma: a clinical and pathological study in 82 patients. *Haematologica*, *101*(8), 976–984. http://doi.org/10.3324/haematol.2016.141978

- NCCN Guidelines: https://www.nccn.org/professionals/physician_gls/f_guidelines.asp#nhl

- ASH Image Bank: http://imagebank.hematology.org/

- https://en.wikipedia.org/wiki/Plasmablastic_lymphoma

- Cover Image: http://www.dovemed.com/diseases-conditions/plasmablastic-lymphoma/