EZH2 expression is dependent on myc and TP53 regulation in diffuse large B-cell lymphoma.

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EZH2 expression is dependent on myc and TP53 regulation in diffuse large B-cell lymphoma.

APMIS. 2020 Jan 28;:

Authors: Neves Filho EHC, Hirth CG, Frederico IAS, Burbano RMR, Carneiro TX, Rabenhorst SHB

Abstract

EZH2 is an important epigenetic regulator, but its role in diffuse large B-cell lymphoma (DLBCL) pathogenesis and its relationship with MYC, BCL2 and TP53 expression, chromosomal rearrangements and clinical features are still poorly understood. So, we investigated EZH2 expression and its associations with the immunophenotypic presentations, including MYC, BCL2 and TP53 expression, MYC, BCL2 and BCL6 translocation status, clinicopathological features and therapeutic response to R-CHOP in a series of 139 DLBCL cases. EZH2 positivity was associated to MYC and TP53 expression (p=0.0002 and p=0.0000, respectively) and to high proliferative index (Ki-67>70%, p=0.0082). No associations were found among EZH2 expression and chromosomal translocation status. The non-germinal center (nGC) DLBCL presented most of associations observed in the general sample; however, only TP53 immunodetection showed associations to EZH2 expression in the germinal center (GC) DLBCL. EZH2 expression had no impact on therapeutic efficacy in R-CHOP treated patients. In conclusion, EZH2 seems to be upregulated by MYC, to rely on TP53 alterations and is associated to high proliferative tumors in DLBCL, which might be dependent on GC or nGC subclassifications. Furthermore, it is not a therapeutic efficacy marker to R-CHOP in our series.

PMID: 31991488 [PubMed — as supplied by publisher]

A Practical Approach to Diagnosis of B-Cell Lymphomas With Diffuse Large Cell Morphology.

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A Practical Approach to Diagnosis of B-Cell Lymphomas With Diffuse Large Cell Morphology.

Arch Pathol Lab Med. 2020 Feb;144(2):160–167

Authors: King JF, Lam JT

Abstract

CONTEXT.—: Large B-cell lymphomas represent the most common non-Hodgkin lymphomas and often present as extranodal masses with advanced stage similar to metastatic tumors. Without proper intraoperative, microscopic, immunophenotypic, and cytogenetic evaluation they may be mistaken for other hematopoietic or even nonhematopoietic tumors. Also, diffuse large B-cell lymphomas often have clinical, morphologic, immunophenotypic, and cytogenetic clinical features that are similar to those of other less common B-cell lymphomas. Furthermore, classification of these neoplasms is continually becoming more refined.

OBJECTIVE.—: To provide a rational, methodic approach to the evaluation of large B-cell lymphomas for community practice pathologists who provide general pathology services.

DATA SOURCES.—: This review incorporates guidelines detailed in the 2017 update to the World Health Organization’s Classification of Tumours of Haematopoietic and Lymphoid Tissues in addition to other recent peer-reviewed publications.

CONCLUSIONS.—: Many large B-cell neoplasms respond favorably to current treatments, but these cases also require accurate and timely diagnoses. We propose a process following a brief checklist that focuses on diffuse large B-cell lymphoma, the most common entity, and rules out other similar lymphomas in a stepwise fashion.

PMID: 31990228 [PubMed — in process]
Poor prognosis in patients with diffuse large B cell lymphomas with bone marrow involvement possessing chromosomal abnormalities, despite aggressive treatment.

Optimizing CAR-T Cell Manufacturing Processes during Pivotal Clinical Trials.

Primary spinal epidural lymphoma: a rare entity with an ambiguous management.
authors report the case of a primary diffuse large B-cell lymphoma of the thoracic spine in a 65-year-old man, who presented to the emergency department with signs of upper motor neuron lesion. The patient underwent surgery in order to decompress the spinal cord. The treatment was concluded with six cycles of chemotherapy with methotrexate, rituximab, cyclophosphamide, vincristine and prednisone followed by radiotherapy. At the 24-month follow-up, no signs of epidural lesion or bone contrast enhancement were observed in thoracic spine MRI. Surgical decompression is recommended in patients with signs of spinal cord injury in order to prevent irreversible neurological damage and is related to high rates of disease-free survival.

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Dissection of DLBCL microenvironment provides a gene expression-based predictor of survival applicable to formalin-fixed paraffin-embedded tissue.


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Lenalidomide in combination with intravenous rituximab (REVRI) in relapsed/refractory primary CNS lymphoma or primary intraocular lymphoma: a multicenter prospective ‘proof of concept’ phase II study of the French Oculo-Cerebral lymphoma (LOC) Network and the Lymphoma Study Association (LYSA).

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Lenalidomide in combination with intravenous rituximab (REVRI) in relapsed/refractory primary CNS lymphoma or primary intraocular lymphoma: a multicenter prospective ‘proof of concept’ phase II study of the French Oculo-Cerebral lymphoma (LOC) Network and the Lymphoma Study Association (LYSA).


Abstract

BACKGROUND: Primary central nervous system lymphomas (PCNSLs) are mainly diffuse large B-cell lymphomas (DLBCLs) of the non-germinal center B-cell (non-GCB) subtype. This study aimed to determine the efficacy of rituximab plus lenalidomide (R2) in DLBCL-PCNSL.

PATIENTS AND METHODS: Patients with refractory/refractory (R/R) DLBCL-PCNSL or primary vitreoretinal lymphoma (PVRL) were included in this prospective phase II study. The induction treatment consisted of eight 28-day cycles of R2 (rituximab 375/m2 i.v. D1; lenalidomide 20mg/day, D1-21 for cycle 1; and 25mg/day, D1-21 for the subsequent cycles); in responding patients, the induction treatment was followed by a maintenance phase comprising 12 28-day cycles of lenalidomide alone (10mg/day, D1-21). The primary end point was the overall response rate (ORR) at the end of induction (P0=10%; P1=30%). RESULTS: Fifty patients were included. Forty-five patients (PCNSL, N=34; PVRL, N=11) were assessable for response. The ORR at the end of induction was 35.6% (95% CI 21.9−51.2) in assessable patients and 32.0% (95% CI 21.9−51.2) in the intent-to-treat analysis, including 13 complete responses (CR)/unconfirmed CR (uCR; 29%) and 3 partial responses (PR; 7%). The best responses were 18 CR/uCR (40%) and 12 PR (27%) during the induction phase. The maintenance phase was started and completed by 18 and 5 patients, respectively. With a median follow-up of 19.2months (range 1.5–31), the median progression-free survival (PFS) and overall survival (OS) were 7.8months (95% CI 3.9−11.3) and 17.7months (95% CI 12.9 to not reached), respectively. No unexpected toxicity was observed. The peripheral baseline CD4/CD8 ratio impacted PFS [median PFS=9.5months (95% CI 8.1–14.8) for CD4/CD8<1.6; median PFS=2.8months, (95% CI, 1.1–7.8) for CD4/CD8