

2018 DOMINICAN HOSPITAL DIFFUSE LARGE B-CELL LYMPHOMA STUDY Patterns of Care and Treatment Compared to Published Treatment Guidelines

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Study population: Diffuse Large B-cell Lymphoma diagnosed and/or treated at Dominican Hospital in 2016 and 2017.

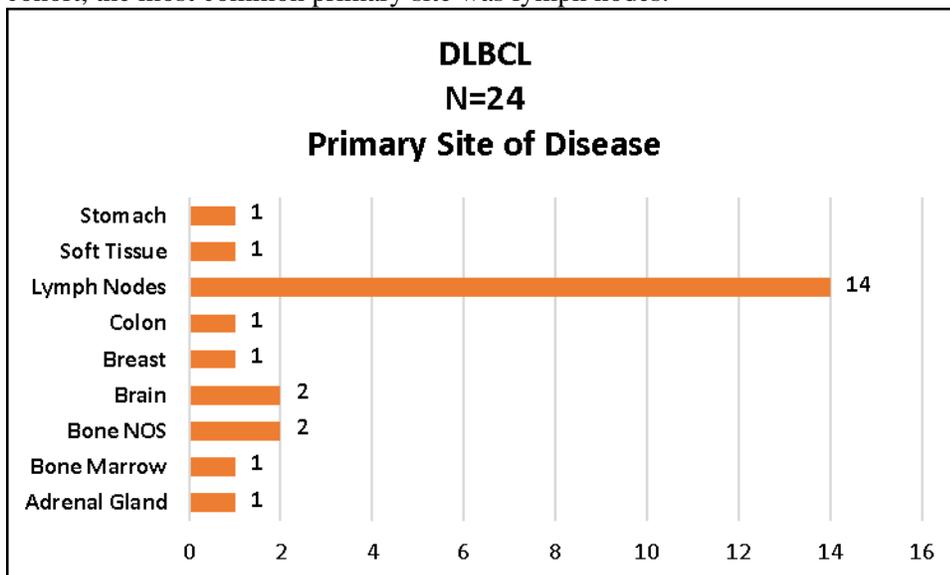
Total number: 24 cases

INTRODUCTION

Diffuse Large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma (NHL) in the United States and worldwide, accounting for up to one-third of patients with newly diagnosed NHL. Despite being an aggressive lymphoma, DLBCL is considered potentially curable. For this study we looked at DLBCL diagnosed in 2016 and 2017, whether molecular analysis was adequately performed and if treatment decisions were altered based on this information. We were especially interested in learning whether these cases were being evaluated for being *double-hit* or *triple-hit* lymphomas and how they were being treated.

PRIMARY SITE

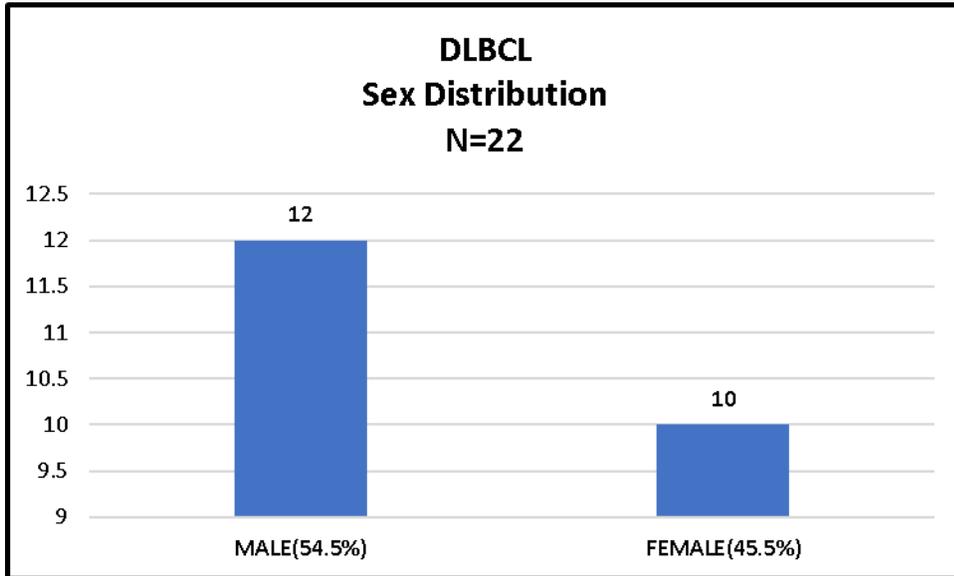
DLBCL most commonly arises in lymph node regions but can also be found in other organs. In this cohort, the most common primary site was lymph nodes.



***The 2 brain primaries will be excluded from subsequent evaluations involving workup and treatment, as primary brain lymphoma is treated differently.**

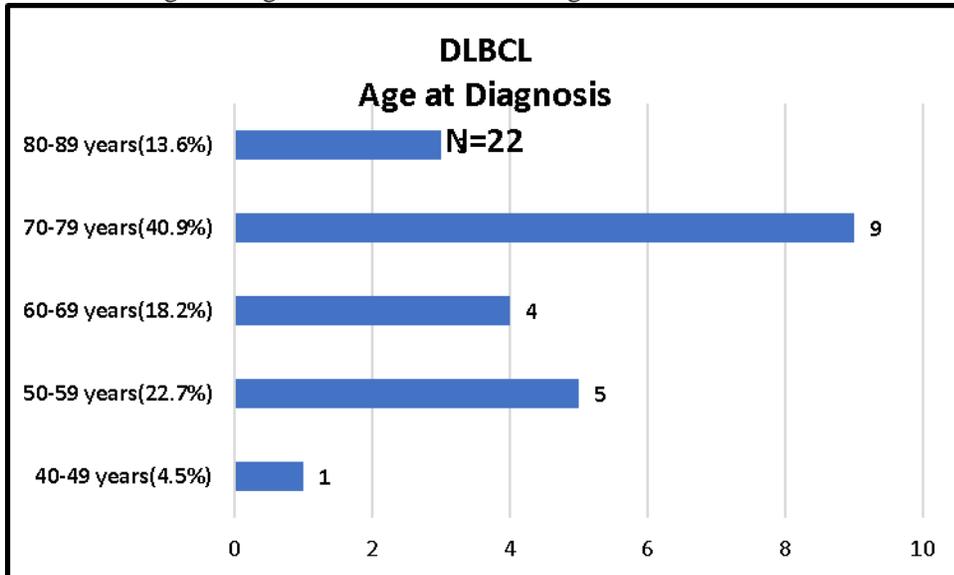
SEX

U.S DLBCL incidence statistics show higher prevalence in men. Our findings are consistent with this statistic.



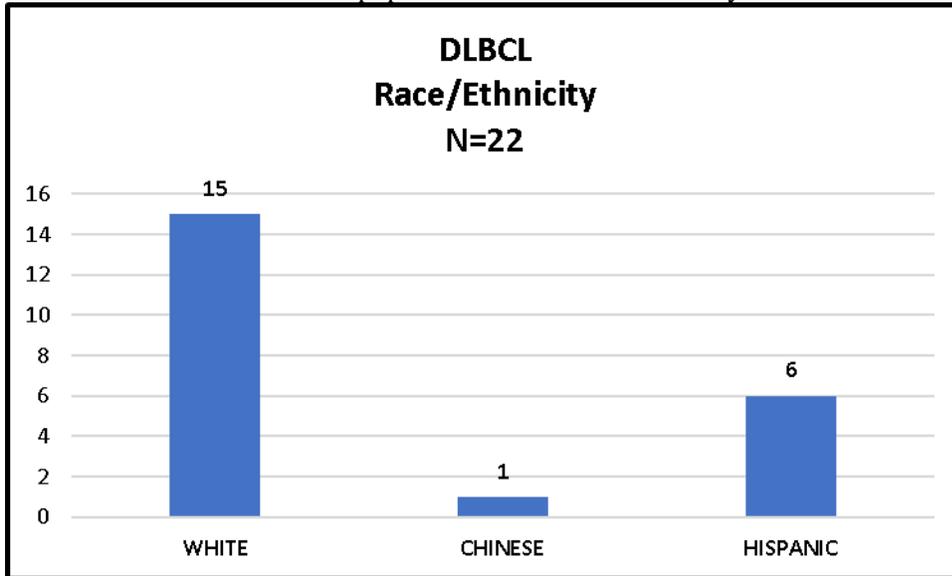
AGE AT DIAGNOSIS

Although it can occur in childhood, the occurrence of DLBCL generally increases with age, and most patients are over the age of 60 at diagnosis. In this cohort, most patients were in the 70-79 age range. The median age at diagnosis was 72, the mean age was 68.



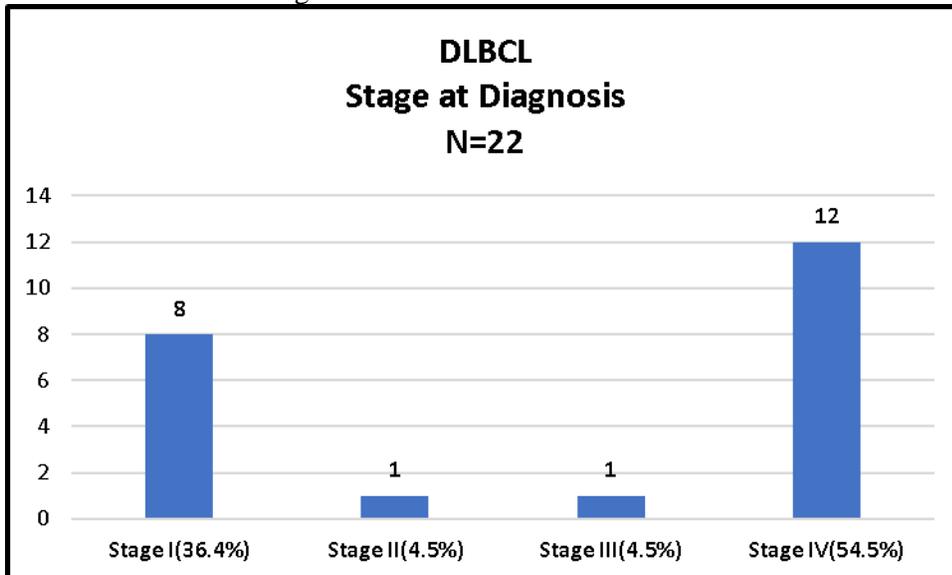
RACE/ETHNICITY

The majority of patients diagnosed and/or treated here were Caucasian at 68%, Hispanic, at 27%, and Asian at 5%. This reflects the population in Santa Cruz County.



STAGE OF DISEASE

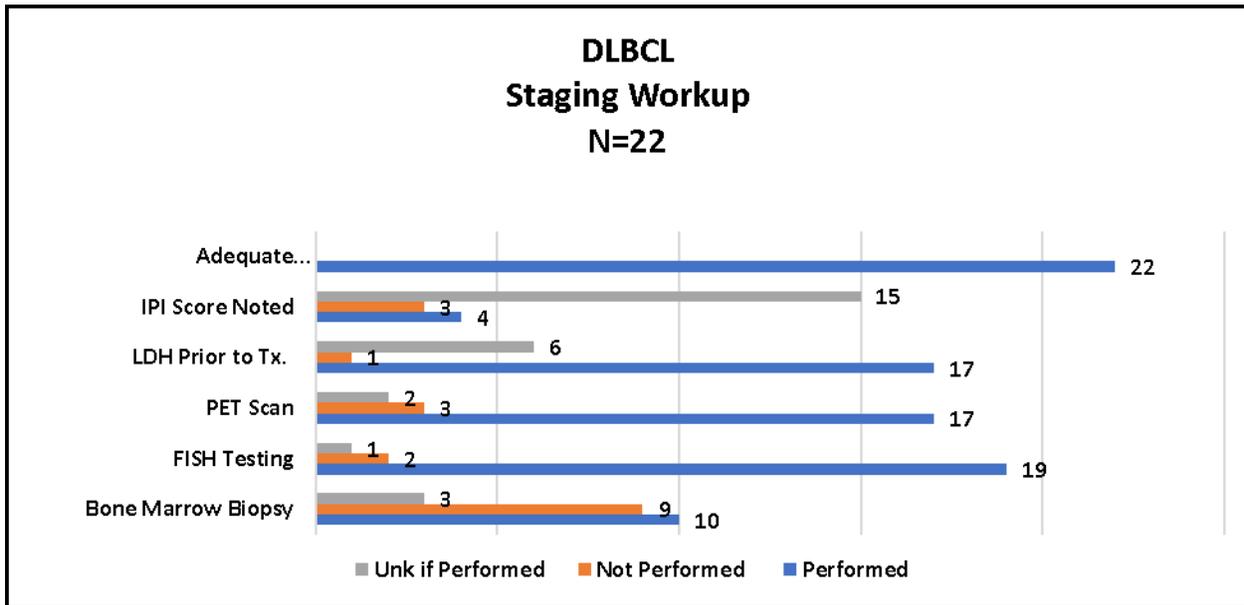
The majority of patients (55%) in this cohort presented with stage IV disease, which includes bone marrow and/or distant organ involvement.



STAGING WORKUP

Although the NCCN lists many essential diagnostic and staging recommendations, we will focus on whether patients had the following:

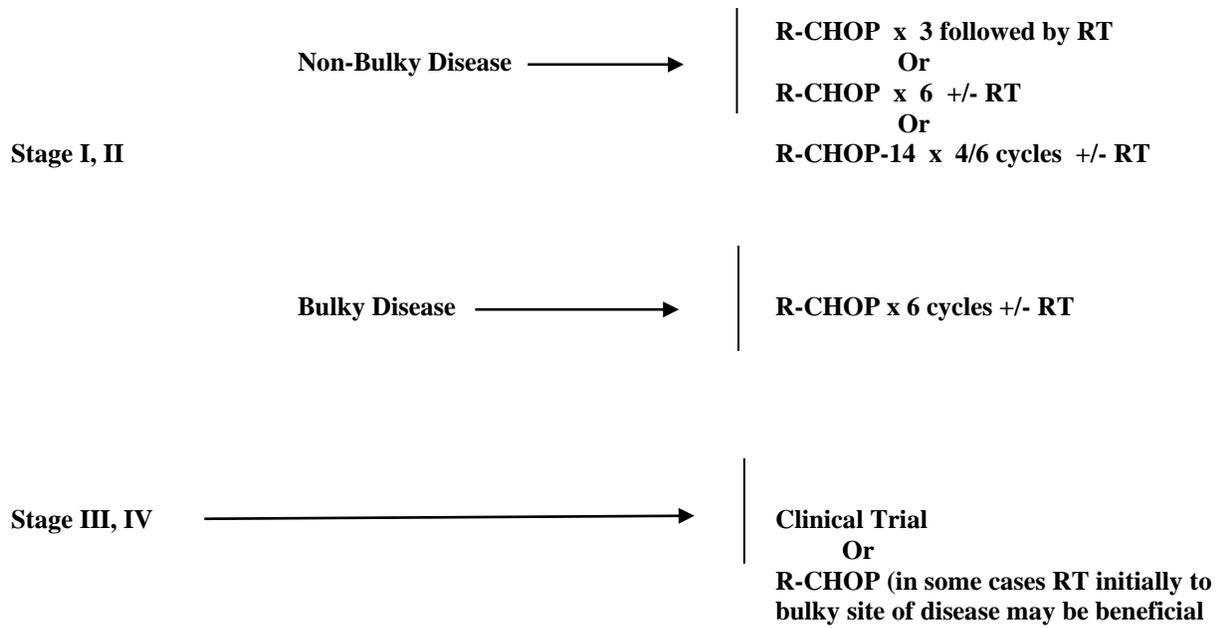
- Adequate immunophenotyping to establish diagnosis
- FISH analysis
- Whole-body PET Scan
- Lactic acid dehydrogenase (LDH)
- Bone marrow aspirate/biopsy
- International Prognostic Index (IPI) Score



***8 patients were excluded from subsequent evaluations because no treatment was administered (1 patient expired, 2 patients chose hospice, 2 patients went elsewhere for treatment and records were not available, 1 patient's pathology could not be confirmed, 2 patients presented with primary brain lymphoma) for a total of 16 remaining patients.**

The majority of patients had documented evidence of diagnostic staging. IPI score was not routinely found in progress notes and physicians discussed the importance of this prognostic tool. Although bone marrow biopsy is on the NCCN list of essential studies, they do give some flexibility based on clinical circumstances and PET scan findings.

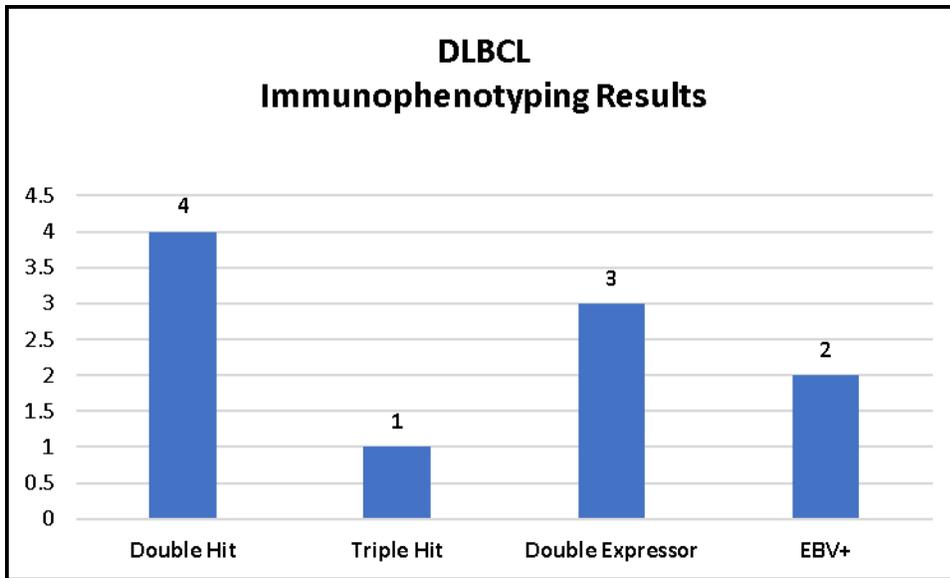
NCCN TREATMENT GUIDELINES FOR DLBCL:



MOLECULAR ANALYSIS: DOUBLE-HIT/TRIPLE HIT AND DOUBLE-EXPRESSOR

The t(14;18) translocation, which involves the rearrangement of *BCL2*, is important in lymphoma and leads to a chemotherapy resistant phenotype. *Double-Hit lymphoma* reflects the presence of both the *MYC* and *BCL2* or *BCL6* gene rearrangements. Rarely, all 3 genes—*BCL2*, *MYC*, and *BCL6*—are simultaneously rearranged in a phenotype termed *triple-hit lymphoma*. Both double-hit and triple-hit lymphomas have a poor prognosis with standard treatment.

Immunohistochemical staining to identify protein expression of these genes show that there are lymphomas in which *MYC* and *BCL2* and/or *BCL6* genes are overexpressed at a protein level, without the genetic rearrangements. Dual-expressor protein, or double protein, refers to immunohistochemical detection of *MYC* and *BCL2* and/or *BCL6* overexpression.



* As a reminder, 1 patient was excluded because the pathology could not be confirmed, as were the 2 primary brain lymphomas.

FINDINGS:

Of the 24 cases accessioned, 8 fell out of the study for various reasons: death, treatment elsewhere, primary brain pathology, etc. Of the remaining 16 patients, all patients were treated with multi-agent chemotherapy as indicated by NCCN guidelines. 4 patients were double-hit, 1 patient was triple-hit, 3 patients were double-expressor, and 2 patients were EBV+.

SUMMARY:

The initial purpose of this study was to evaluate if DLBCL was being treated according to published guidelines and evaluate if FISH analysis for gene rearrangement was being done regularly in our Dominican DLBCL cases, and whether that changed the treatment regimen for those cases.

1/16 evaluable cases did not have FISH done on the diagnostic biopsy of bone marrow because it was sent to Neo-Genomics and they do not routinely do FISH for gene rearrangements. All other DLBCL biopsy sites are routinely sent to Stanford where FISH is always done.

Although there is no definitive clinical trial, our local oncology thought leaders usually recommend dose adjusted R-EPOCH for double hit or triple hit DLBCL.

- 2/4 double hit patients were treated with this regimen, the other 2 were treated with standard R-CHOP.
- 1 triple hit patient went elsewhere for treatment and records were not available.
- 1/3 Double-expressor patients were treated with R-CHOP, and 2/3 were treated with R-EPOCH.
- 1/2 EBV+ patients went directly to hospice following diagnosis and did not receive treatment.
- 1/2 EBV+ patients were treated with R-CHOP+intrathecal methotrexate as CNS prophylaxis.

RECOMMENDATIONS:

Our medical oncologists seem to be extremely knowledgeable in current treatment guidelines and recommendations and are aware of the importance of immunophenotyping in treatment decisions. All oncologists will be notified that when the diagnostic biopsy on a DLBCL case is on bone or bone marrow and sent to Neo-Genomics, if they are concerned about *MYC*, *BCL2* or *BCL6* gene rearrangements, they will need to request FISH testing specifically as this is not routinely performed. No further recommendations needed as study results are satisfactory.

REFERENCES:

<https://www.lymphoma.org/aboutlymphoma/nhl/dlbcl/>

https://www.nccn.org/professionals/physician_gls/pdf/b-cell_blocks.pdf

<http://www.hematologyandoncology.net/archives/january-2017/aggressive-b-cell-lymphoma-the-double-hit-and-double-expressor-phenotypes>