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A potential role of Ibrutinib in stage IV highly aggressive Activated B Cell type Diffuse Large B Cell Lymphoma (ABC DLBCL)

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INTRODUCTION

This case report enlightens the subgroup analysis of Phase III, PHOENIX trial, where using Ibrutinib with R-CHOP in patients with stage IV ABC-DLBCL showed improved event-free survival (EFS), progression-free survival (PFS) and overall survival (OS) in ABC DLBCL patients aged 60 or younger[2], despite the trial being a negative study otherwise.

CASE DESCRIPTION

- A 31-year-old female presented to the emergency department, for six weeks of onset of diffuse back pain, abdominal pain, headaches, facial weakness, and 20 lbs unintentional weight loss.
- Pertinent findings showed CT abdomen/pelvis w/wo contrast a bilateral renal mass, right adrenal mass, extensive retroperitoneal adenopathy, compatible with advanced process, and negative chest imaging.
- A renal mass biopsy showed a background of a "starry sky" seen by apoptotic bodies within histiocytes, and immunohistochemistry was positive for double hit rearrangement, Neg EBER, confirming ABC type DLBCL.
- The patient was started on R-CHOP, and PET/CT followed by 1st cycle showed radiographic improvement in nephromegaly and necrotic retroperitoneal adenopathy, however, continued to have a lot of body pain, headaches, and weight loss. CSF studies confirmed lymphomatous spread and her symptoms did not improve despite IT Methotrexate.
- We added Ibrutinib with the next R-CHOP cycle as suggested by the PHOENIX trial and she showed tremendous improvement in her symptoms.

DISCUSSION

- The ABC DLBCL is known to have worse outcomes, ~ 5-10% have double-hit lymphoma-rearrangement between MYC and BCL2 and/or BCL6 protein, and when associated with carcinomatous leptomeningeal involvement, has further a poor prognosis.1
- ABC DLBCL has aberrant activation of several signaling pathways including the B cell receptor signaling pathway and targeting BTK, a key component of the BCR pathway, inhibiting downstream signaling may further reduce the proliferation and survival of malignant B cells.
- Ibrutinib-BTK inhibitor that has been approved for treating several B cell malignancies, i.e., mantle cell lymphoma, phase III trial-PHOENIX trial performed to see its potential for DLBCL. Despite Ibrutinib not showing promising results in the primary endpoint of the trial, our case does fit that subgroup of patients mentioned in the trial, who are below age <60 years, with ABC type DLBCL to have benefits EFS, PFS, and OS2 and aid achieving remission. Further meta-analysis on these treatments is required.

Fig. 1: Pathways Targeted By Treatments Currently in Development for Patients with DLBCL

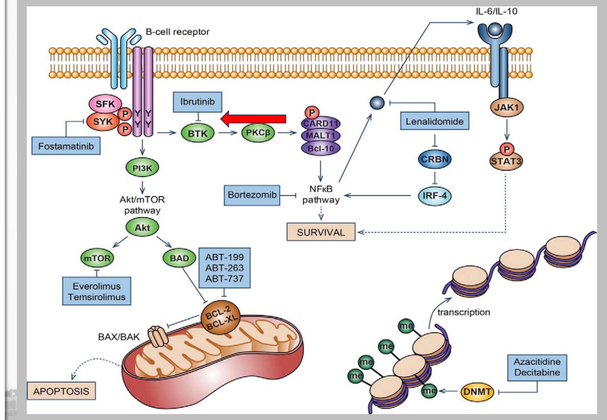


Fig. 2: Kaplan-Meier survival curves for EFS and OS by cutoff of age 60 years in the intent-to-treat population. (A) EFS, age younger than 60 years (n = 342). (B) OS, age younger than 60 years (n = 342). (C) EFS, age 60 years or older (n = 496). (D) OS, age 60 years or older (n = 496).- PHOENIX Trial

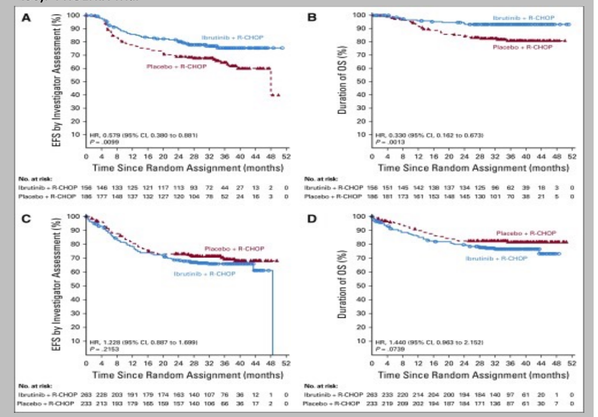


Fig. 3: Medium to large cells with a diffuse chromatin pattern and a nucleoli. A background of a "starry sky" is present as seen by apoptotic bodies within histiocytes.

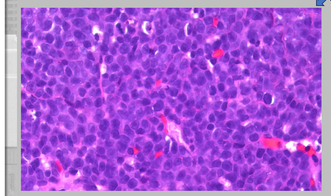


Fig. 4: IHC stain: CHD20, 79 a, MUM1, BCL2, BCL6, Ki-67 90%, EBER neg, Activated B cell subtype by Hans criteria

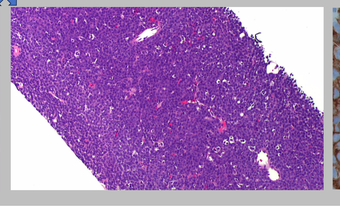
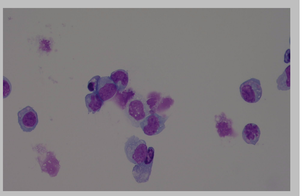


Fig 5. Malignant Lymphoma cells present in CSF



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