Response to Bruton's Tyrosine Kinase Inhibitors in Light Chain Amyloidosis caused by Lymphoplasmacytic Lymphoma

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Declarations of Interest: None

Funding source: None

Word Count: 305

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Abstract

Introduction:

IgM related light chain (AL) amyloidosis represents around only 5% of all light chain amyloidosis with around 10-22% of cases associated with Waldenstrom macroglobulinemia or multiple myeloma. Chemoimmunotherapy, proteosome inhibitors , immunomodulators along with autologous stem cell transplantation have been the primary treatment modalities used in light chain amyloidosis. We explore the use of Bruton's tyrosine kinase (BTK) inhibitors, ibrutinib and acalabrutinib, in patients with IgM AL amyloidosis.

Materials and Methods:

We retrospectively evaluated the effect BTK inhibitors, ibrutinib and acalabrutib in 4 patients with IgM-related AL amyloidosis with underlying WM. Gender distribution was equal (two males and two females), with a median age of 73 (range 60-91) at the time of BTK therapy initiation. Detection of MYD88 mutation was present in all patients. Three out of four patients received a BTK inhibitor as a first-line treatment. Two patients received ibrutinib and the other two received acalabrutinib. Three patients exhibited cardiac, renal and hepatic involvement; only one exhibited renal involvement by underlying AL amyloidosis.

Results:

Figure 1 reveals the difference in free light chains before and after BTK therapy. Figure 2 reveals the drop in IgM after BTK initiation.

Two patients achieved very good partial response and the other two had a complete response based on consensus criteria. No significant side effects were reported, apart from mild peripheral neuropathy, mild gingival bleeding, and a subungual hematoma. Ibrutinib was discontinued due to atrial fibrillation in a patient with cardiac amyloidosis. Two patients with cardiac amyloidosis who received acalabrutinib tolerated the medication with no cardiac arrhythmia.

Conclusion:

BTK inhibitors, ibrutinib and acalabrutinib, are highly active and may yield long-term disease control as a first-line treatment, when used in combination with rituximab in patients with IgM related AL amyloidosis and WM. Reported side effects were mild, and the treatment was well tolerated. Patients with cardiac AL amyloidosis may tolerate acalabrutinib better than ibrutinib.

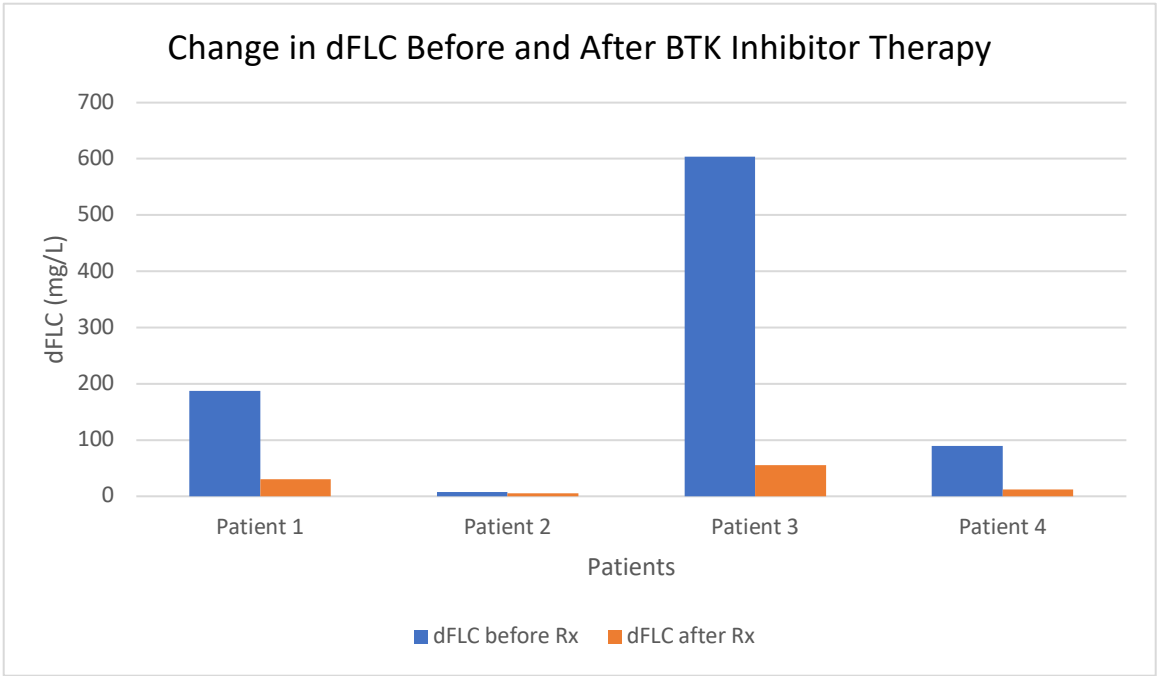

Figure 1. Change in difference of free light chains before and after BTK inhibitor therapy.

dFLC: difference in free light chain, Rx: Therapy

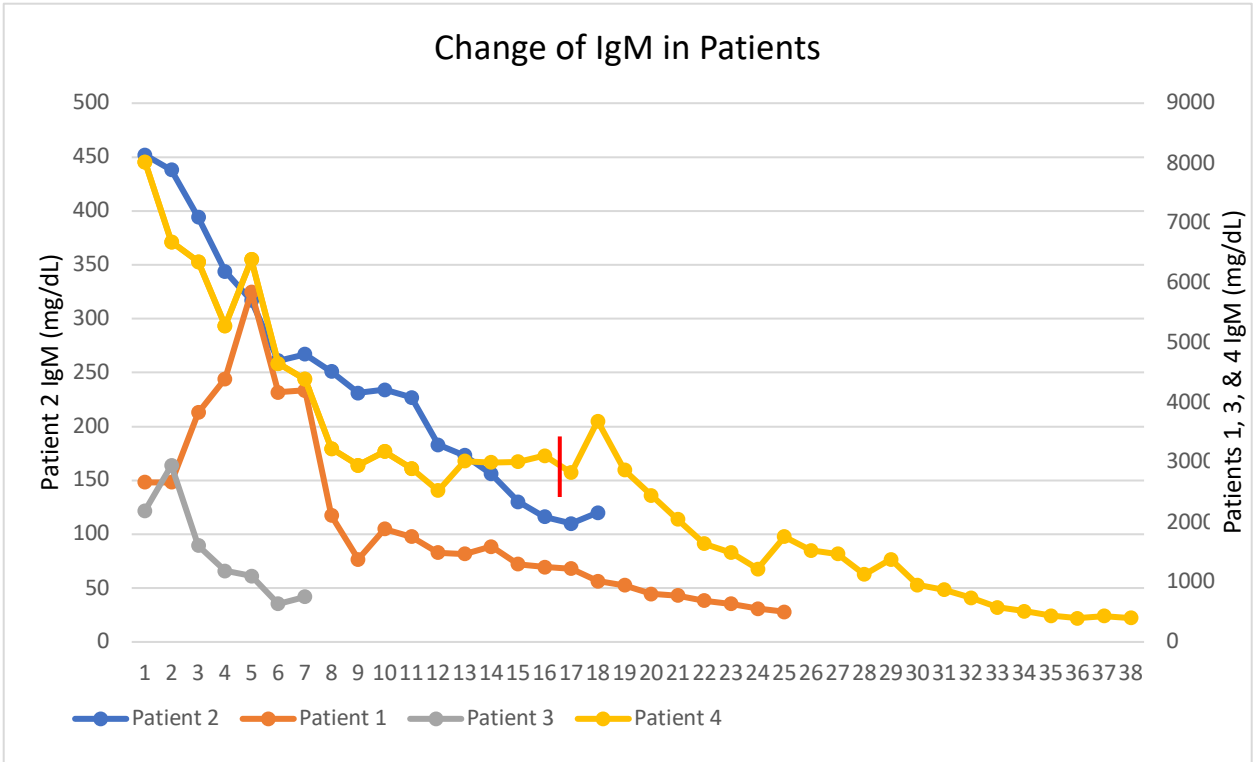

Figure 2. Change of IgM in patients. The red line indicates the initiation and termination of BTK inhibitor in patient 4.