Ibrutinib for the Treatment of Bing-Neel Syndrome

G. Itchaki¹, J. Paludo², S. Ansell³, L. Palomba³, S. Treon¹, J. Castillo¹

¹Dana-Farber Cancer Institute, Boston, MA, USA; ²Mayo Clinic, Rochester, MN, USA; ³Memorial Sloan Kettering Cancer Center, New York, NY, USA

Background
- Bing-Neel syndrome (BNS) is a rare complication of Waldenstrom macroglobulinemia (WM), in which WM cells gain access to the CNS causing neurological deficits¹.
- Treatment options in patients with BNS are limited
- Ibrutinib, an oral BTK-inhibitor, and the only approved therapy in WM, can penetrate into the CNS², but data on BNS is lacking.

Aim
To evaluate the efficacy of ibrutinib in patients with BNS

Methods
- Retrospective study in 2 centers
- Diagnosis of BNS was established in pts with WM by radiological and/or cytological evidence of CNS involvement by WM
- Response was assessed based on recently published criteria³
- Ibrutinib was given at 420-560 mg PO qd until disease progression or intolerable toxicity

Results – Patients Characteristics
- 11 patients are reported; median age @ WM diagnosis was 60 years (48-73)
- Median lines of therapy for WM prior to BNS diagnosis was 2 (0-7);
- 4 patients (36%) were untreated prior to BNS
- The median age @ BNS diagnosis was 65 years (49-78), with a median of 6.6 years from WM to BNS diagnosis (0.1-15)
- Most common BNS symptoms were motor (n=7), sensory (5), and cognitive (4) deficits, and seizures (3).
- MRI findings included leptomeningeal enhancement (6) and brain masses (4)
- CSF cytology was positive in 7 pts, confirmed by flow cytometry in all 7.
- Biopsies were performed in 3 patients and confirmed Dx
- Dx was based on MRI only in 1 pt
- Median serum IgM prior to ibrutinib initiation was 1218 mg/dl (range 616-3330 mg/dl), and Hb was 11.8 g/dl (9.2-15 g/dl).
- Median lines for BNS prior to ibrutinib was 1 (0-4); it was the first line in 5 pts

Response Assessment
- Symptoms improved in 8 of 9 patients with available data
- At best response, median IgM and Hb levels were 384 mg/dl (222-3330 mg/dl) and 13.3 g/dl (range 9.2-15 g/dl), respectively.
- MRI findings improved in 7/8 patients and were stable in 1
- CSF studies cleared in 2 patients and were stable in 2 patients.
- To date, 4 pts have stopped ibrutinib: 2 with PD - next lines were MTX/TMZ and FR; 1 d/t intolerance for BNS (→ BR); and 1 died with suspected BNS progression.

Conclusion
- Ibrutinib is a safe and effective treatment option for patients with BNS

References

Corresponding author: Jorge_Castillo@dfci.harvard.edu
There are no relevant conflicts of interest to disclose