Promising Efficacy Signal in Secondary CNS Lymphoma Patients Treated with Emavusertib and Ibrutinib

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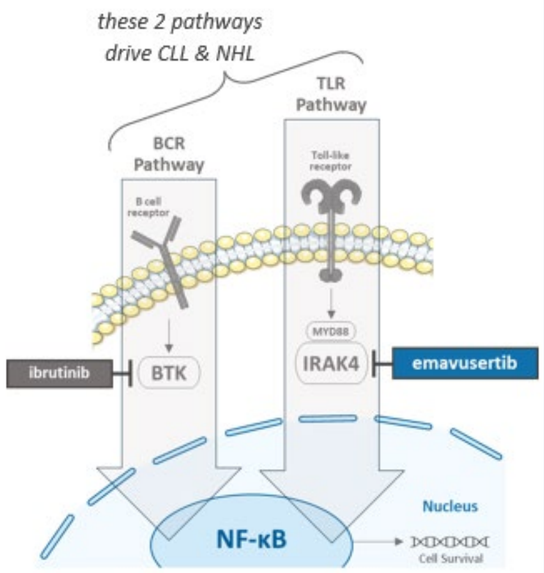
BACKGROUND

Secondary central nervous system lymphoma (SCNSL) is defined as the diagnosis of CNS lymphoma diagnosed concurrently with systemic lymphoma or after prior treatment. Due to the poor prognosis associated with SCNSL, the lack of randomized trial data, and the need for international consensus guidelines, there is a high unmet need for effective therapy options for SCNSL.

OBJECTIVE

Here we present safety and efficacy data on 2 SCNSL patients treated with the combination of emavusertib and ibrutinib. Both patients had directly progressed on their prior BTKi treatment. One patient achieved an unconfirmed complete response (CRu) and remained on treatment for over 4 mos, while the other patient maintained stable disease (SD) with a 38% reduction in disease burden from baseline and was on treatment for more than 8 mos.

MECHANISM OF ACTION



CLL and NHL

dual blockade of NF-kB enables stronger downregulation of NF-kB and deeper responses

PATIENT #1

Baseline Characteristics:
65-year-old white male. Diagnosed with SCNSL in April 2015 from primary testicular lymphoma.

Medical History:

Hypothyroidism, gastritis, low testosterone, chronic kidney disease, migraine headache, and herpes zoster.

Pathology:

Diffuse large B-cell lymphoma, CD10 positive, CD20 positive, coexpressing BCL-6. Negative for BCL-2 and MYC

Prior Therapy:

2015/16 – R-CHOP with MTX (6 cycles)

Dec 2019 - Feb 2020 – MTX with rituximab

Feb 2020 – Apr 2020 – Topotecan, MTX, etoposide, cytarabine, trastuzumab with radiation and consolidative ASCT

Sep 2021 – Intrathecal cytarabine, MTX, hydrocortisone

Nov 2021 – Ibrutinib

Response:

Patient started on emavusertib 300 mg twice daily with ibrutinib 560 mg daily in December of 2021. He achieved stable disease response through August of 2022. He remained on combination therapy for 253 days total. Best response throughout was SD. Patient discontinued therapy due to hyperglycemia which was not attributed to therapy.

Treatment-Related Side Effects (≥Grade 3):

Grade 3 AST/ALT, Blood Bilirubin Increase. These were reversible and managed with standard supportive care.

Change in Disease Burden:

-38%

CONCLUSIONS

- The 2 patients presented here are supportive data for utilization and continued research into the clinical efficacy of the combination of emavusertib with a BTK inhibitor (ibrutinib) in SCNSL.
- In each case, the patient had previously progressed while being treated with a BTK inhibitor and the addition of emavusertib resulted in 1 CR and 1 SD.

PATIENT #2

Baseline Characteristics:
75-year-old white male. Initially patient had systemic disease including involvement in the adrenal glands, vitreous, and CNS with diagnosis in March of 2018. He subsequently had isolated CNS relapse in November of 2020.

Medical History:

Chronic kidney disease, diabetes mellitus type 2, pulmonary embolus, GERD, NSTEMI, hypothyroidism, hyperlipidemia, hypertension

Pathology:

Diffuse large B-cell lymphoma BCL2 negative and MYC positive by IHC. Negative for MYC gene rearrangement by FISH analysis.

Prior Therapy:

2018 – MR-CHOP

2020 – MRT with consolidative ASCT

2023 – MRT

February 2024 – Ibrutinib

Response:

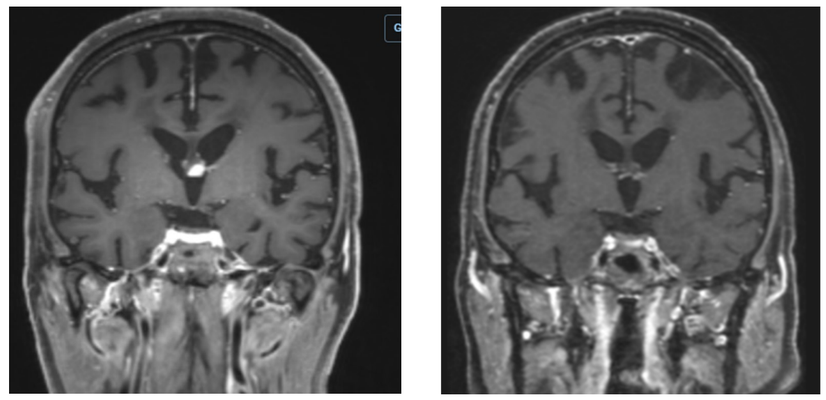
Patient started on emavusertib 150 mg twice daily with ibrutinib 560 mg daily in December of 2024. He was increased to 200 mg twice daily dose of emavusertib shortly after initiation. He achieved complete response noted on MRI in February of 2025. Due to side effects of emavusertib, dose was reduced by 50 mg daily increments. Patient ultimately discontinued therapy due to progression of disease in April of 2025. He was on combination therapy a total of 109 days.

Treatment-Related Side Effects (≥Grade 3):

Grade 3 hypoglycemia. Grade 4 neutropenia. These were reversible and managed with standard supportive care.

Change in Disease Burden: -100%

MRI



MRI on the left taken before starting emavusertib shows an 8 x 8 x 5 mm lesion about the anterior pillar of the fornix. The MRI on the right was completed 6 weeks after starting treatment and show CR.