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POSTER ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

A Single Arm Phase II Pilot Study of Low Dose Vemurafenib Plus Rituximab in the Front-Line and Relapsed/Refractory Treatment of Hairy Cell Leukemia

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Introduction: Hairy Cell Leukemia (HCL) is a rare, low-grade B-cell malignancy that is characterized by cytopenias, infections and splenomegaly. Given the chronic and incurable nature of this disorder, limiting therapy-related toxicity is of paramount importance. Though purine nucleoside analogs have an established track record of durable efficacy, they are associated with significant myelosuppression and immunosuppression as well as late secondary malignancies. Mechanistic exploitation of aberrant BRAF V600E activation with vemurafenib in combination with CD20 targeting with rituximab has provided an effective means of eradicating leukemic cells without significant myelosuppression or immunosuppression. However, vemurafenib at the standard dose of 960 mg twice daily is often poorly tolerated and frequently requires dose reduction. We conducted a pilot study of rituximab and low-dose vemurafenib (240 mg twice daily) in patients with untreated or relapsed HCL, with a focus on providing a non-cytotoxic regimen that minimizes toxicity with potentially comparable treatment outcomes.
Methods: This phase 2, open-label, single-arm, investigator-initiated pilot trial was designed, conducted, and managed at Scripps Clinic in La Jolla, California. We enrolled adult patients with HCL and mutated BRAF V600E who met standard treatment initiation criteria defined by an ANC $\leq$1.0, Hgb $\leq$ 10.0 or PLT $\leq$100K. The treatment plan consisted of eight weeks of oral vemurafenib 240 mg twice daily and eight intravenous rituximab infusions at 375 mg per square meter of body-surface area administered every two weeks. The primary outcome was complete hematologic response. Secondary endpoints included time to complete hematologic response, clearance of minimal residual disease determined by BRAF V600E allele frequency in the bone marrow, safety and progression-free, relapse-free and MRD-free survival.
Results: From March 2022 to July 2023, a total of six patients were enrolled in the study. Three patients had previously received a purine analog and three patients were previously untreated. The median age of patients was 61 years, and all were male. At the interim efficacy analysis, all five (5/5) evaluable patients had demonstrated a complete hematologic response with resolution of cytopenias and splenomegaly. 6-month bone marrow biopsy data were available for 3 patients. In 2 of these patients, MRD assessment by allele-specific PCR for BRAF V600E was absent in the bone marrow. In the third patient, though residual disease was present by MRD assessment, he had a hematologic response and requires no subsequent treatment to date. At a median follow-up time of 303 days, the relapse-free survival rate was 100%. There were no adverse grade 3 or 4 adverse events and no vemurafenib dose limiting toxicity was observed.
Conclusions: Interim results to-date suggest that rituximab and low-dose vemurafenib (240 mg twice daily) have efficacy and good tolerability in patients with untreated or relapsed HCL. With accruing patient data and further enrollment on study, more information will guide the durability, efficacy and tolerability of this treatment approach.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: Neither vemurafenib nor rituximab are approved by the Food and Drug Administration for the treatment of hairy cell leukemia

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