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Abstract 3662 Open-Label Bendamustine Combined with Rituximab for Treatment of Relapsed/Refractory Mantle-Cell Lymphoma: Efficacy and Safety Findings

Myron S. Czuczman, MD[1], Dominick Lamonica, MD[2*], Shari K. Gaylor[3*], Leonard Bush, BHS[4*], Penny Nadolny[5*] and Dave Colborn[6*]

[1]Roswell Park Cancer Institute, Buffalo, NY
[2]Nuclear Medicine, Roswell Park Cancer Institute, Buffalo, NY
[3]Veeda Oncology, Columbus, OH
[4]Clinical Data Management, Veeda Oncology, Columbus, OH
[5]Monitoring Services, Veeda Oncology, Columbus, OH
[6]Clinical Data Management & IT, Veeda Oncology, Columbus Ohio, OH

Background

Mantle-cell lymphoma (MCL) is an aggressive non-Hodgkin lymphoma (NHL) subtype, typically presenting as stage IV disease. There is no established standard of care; chemotherapy usually results in a tumor response, but cure is rare and the median survival is 3 to 5 years. Bendamustine, a unique alkylating agent, and rituximab, an anti-CD20 monoclonal antibody, showed respective overall response rates (ORR) of 75% and 92% in 16 and 12 patients with relapsed/refractory MCL in two open-label, phase 2 clinical trials on NHL and MCL.

Methods

This 24-week, multicenter, phase 2 study included adults with relapsed/refractory, CD20-positive, B-cell MCL (nonblastoid) who received ≤3 prior chemotherapies. Patients received intravenous (IV) bendamustine 90 mg/m^2 on days 1 and 2 and IV rituximab 375 mg/m^2 on day 1 (except patients with an absolute lymphocyte count >5 x 10^9/L that in cycle 1, received rituximab across 3 days and bendamustine on days 3 and 4) for six 28-day treatment cycles (up to 8 cycles for those without disease progression [PD] and without a documented complete response [CR]). Patients received analgesics/antipyretics prior to rituximab administration. The primary efficacy measure was ORR (CR + partial response [PR]). Secondary efficacy measures included duration of response, progression-free survival (PFS), overall survival (OS), and rate of conversion from positron emission tomography (PET)-positive to PET-negative disease. Safety measures included adverse events (AEs). Data from treatment cycles 7 to 8 were included only in the safety analysis.

Study enrollment was terminated by the sponsor for nonclinical reasons. Data analysis is ongoing, and final data will be presented.

Results

Of 45 patients, median age was 71 (range 48-88) years. Median number of prior chemotherapies was 1 (range 1-3). Seven patients discontinued study treatment early (2 each during cycles 2 and 3; 1 each during cycles 1, 5, and 7); 2 patients withdrew consent from the study, 2 discontinued due to AEs (thrombocytopenia; back pain; grade 5 myocardial infarction, pneumonia, and respiratory failure), and 3 due to PD. Median treatment duration was 6 (range 1-8) cycles.

ORR was 82% (38% CR, 44% PR) (90% CI 70.2%-90.8%); median duration of response was 14.5 months (range 11.3 months to not reached). Median PFS was 16.4 months, with 1-year PFS rate of 62%. Median 3-year OS has not been reached by Kaplan-Meier analysis. Image-based metabolic profiling in analysis of response is ongoing.

Eleven patients (24%) had a bendamustine dose reduction, but no patient had a rituximab dose reduction. There were a total of 24 delayed treatment cycles (median 1, range 0-3), 83% of which had ≤21 days of delay. The most common reasons for dose reduction/delay were neutropenia (n=11) and thrombocytopenia (n=8). Seventeen patients had serious AEs; the most frequent were pneumonia (n=3), confusional state (n=2), and pleural effusion (n=2), which were considered unrelated to bendamustine. Grade 3/4 hematologic laboratory toxicities were lymphopenia (n=40), neutropenia (n=20), leukopenia (n=20), thrombocytopenia (n=3), and anemia (n=2). The most common nonhematologic grade 3/4 AEs were hypokalemia and hypotension (n=3 each). There were 8 patients with grade 3/4 infections and infestations (any term). Four patients (9%) had an infusion-related reaction, and 22 patients (49%) received growth factors during treatment. One death occurred during the study due to myocardial infarction, pneumonia, and respiratory failure; this was considered to be unrelated to study treatment.

Conclusions

Bendamustine plus rituximab showed a high ORR with a long duration of response. It was adequately manageable in patients with relapsed/refractory MCL, with a low rate of infusion-related reaction.

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Disclosures: Czuczman: *Mundipharma:* Honoraria; *Genentech:* Consultancy. **Off Label Use:** Bendamustine is FDA-approved for adults with chronic lymphocytic leukemia or indolent B-cell non-Hodgkin's lymphoma that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.. **Lamonica:** *Teva:* Consultancy. **Gaylor:** *Veeda Oncology, which received research funding from Teva*

Pharmaceuticals: Employment, Research Funding. **Bush:** *Veeda Oncology, which received research funding from Teva Pharmaceuticals:* Employment, Research Funding. **Nadolny:** *Veeda Oncology, which received research funding from Teva Pharmaceuticals:* Employment, Research Funding. **Colborn:** *Veeda Oncology, which received research funding from Teva Pharmaceuticals:* Employment, Research Funding.

[*] *signifies non-member of ASH*