Bendamustine HCl (TREANDA™) Treatment in Combination with Rituximab Results in Objective Responses in Patients with Refractory/Relapsed Indolent B-Cell and Mantle Cell Non-Hodgkin's Lymphoma: Results from Phase II Multicenter Study (SDX-105-02).

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Background: Bendamustine hydrochloride (SDX-105; Treanda™) is a multifunctional, alkylating agent with a purine-like ring system and novel mechanisms of action that exhibits impressive single-agent activity in multiple hematologic and solid tumors. *In vitro* data indicate that bendamustine induces cell death as a result of both apoptosis and mitotic catastrophe, resulting in potent cell-killing activity in cancer cells that are resistant to traditional chemotherapy (alkylating and fludarabine-containing regimens). *In vitro* data have also demonstrated a synergistic effect with rituximab for the treatment of non-Hodgkin's lymphomas (NHL). A Phase II multicenter study (SDX-105-02) was conducted to determine the efficacy and toxicity of the combination of bendamustine with rituximab in relapsed NHL patients.

Methods: The intent-to-treat (ITT) population consists of 54 patients with relapsed indolent CD20-positive B-cell or mantle cell NHL, enrolled from 22 sites in the US and Canada. Median age of the patients was 60 years (range 40-84); 59% had follicular NHL, 6% had small lymphocytic lymphoma, 4% had lymphoplasmacytoid lymphoma, 4% had marginal zone lymphoma, and 17% had mantle cell lymphoma; and 72% of all patients had Stage III/IV disease. Patients relapsed from a median of 1 prior therapy. Patients received rituximab, 375 mg/m² IV on day 1, and bendamustine, 90 mg/m² on days 2 and 3, every 28 days for 4-6 cycles. All patients received an additional dose of rituximab 1 week prior to the first cycle of bendamustine and 4 weeks after the last cycle. Results: Of the 54 ITT patients, 37% had prior treatment with rituximab. Forty-three patients are currently evaluable for response, as defined by the International Working Group. The overall response rate was 84%, with complete response in 21% and partial response in 63% of patients. The median duration of response has not yet been reached after a median follow up of 3.6 months. Minimal toxicity was observed. The most common nonhematologic toxicities included grade 1/2 gastrointestinal complications. The primary grade 3/4 hematologic toxicity was neutropenia (with no neutropenic fever), observed in 22% of patients. Grade 3/4 anemia and thrombocytopenia were observed in only 1 patient. No alopecia was observed. Conclusions: Bendamustine, administered in combination with rituximab, produced high objective response rates with minimal toxicity in patients with refractory indolent and mantle cell NHL, including patients that previously failed alkylating and fludarabine-containing regimens. A Phase III trial with bendamustine as a single agent in patients with rituximab-refractory indolent NHL is ongoing.

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