2691 Single Agent Bendamustine Is An Effective Pre-Vaccine Treatment for Patients with Relapsed Follicular Lymphoma Undergoing Idiotypic Vaccination

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Over the last two decades, idiotypic vaccination has shown evidence of biological efficacy, clinical efficacy and clinical benefit in some subsets of patients with follicular lymphoma. Despite this, no idiotype vaccine has yet obtained regulatory approval. A phase-I clinical trial is currently being conducted to assess safety and immunogenicity of therapy with bendamustine and prednisone (BP) followed by administration of a novel, recombinant idiotype vaccine inwhich the idiotype protein is produced in tobacco plants. Patients eligible for the study are those with relapsed follicular lymphoma whose prior treatment has included rituximab. Use of rituximab is prohibited in this trial due to its potentially negative interference with vaccination as a consequence of the prolonged B-cell depletion that characteristically follows its administration. Subjects enrolled in the study who achieve and maintain either a complete (CR) or partial (PR) response for at least 4 months following BP therapy undergo idiotype vaccination. The response to initial BP therapy prior to vaccine administration is the subject of this report.

At the time of abstract submission, fourteen patients have completed four monthly cycles of bendamustine (120 mg/m2 IV on day 1 and 2) and prednisone (100 mg PO on day 1 through 5). Of the thirteen patients evaluable for clinical response, eleven (85%) have achieved a CR and two (15%) a PR. Six patients maintained their response for at least 4 months and went on to receive idiotypic vaccine. The other six patients are currently in the 4-month protocol specified off-therapy period between chemotherapy and vaccination. One patient, who achieved a CR, relapsed during this period and was not vaccinated. With this exception, and with an overall median follow-up of 5 months (range: 2-12 months), all other responses described above have been maintained.

Currently, toxicity data are available for 54 cycles of BP. There was no grade 4-5 non-hematologic toxicity. Grade 3 non-hematologic toxicity was recorded in 5/14 (36%) patients and in 9/54 (17%) cycles, respectively, and included hyperglycemia, diarrhea, nausea, dehydration and hypotension. Grade 1-2 non-hematologic toxicities were relatively common and in line with those previously reported for the BP regimen. Only 1/54 BP cycles was delayed due to grade neutropenia. In this case, the planned cycle was administered two weeks later. Overall grade 4 hematologic toxicity was recorded in 4/14 (14%) patients and in 7/54 (13%) cycles, respectively, and included neutropenia andlymphopenia. Grade 3 hematologic toxicity was recorded in 9/14 (64%) patients and after 21/54 (39%) cycles, respectively, and included leukopenia,

neutropenia, lymphopenia and thrombocytopenia. Overall, lymphopenia was the most common grade 3-4 hematologic toxicity. Grade 1-2 hematologic toxicities were common, expected, and included anemia, leukopenia, neutropenia, lymphopenia and, occasionally, thrombocytopenia.

Data are available for four patients to analyze post-chemotherapy B- and T- cell recovery.

Patient	lymphocytes/ml		CD3(+)		CD4(+)		CD8(+)		CD19(+)	
nlrange	1000-4000		960-2600		540-1660		270-930		122-632	
	pre*	post*	pre	post	pre	post	pre	post	pre	post
A	713	1166	471	770	228	140	250	595	36	18
B	8892	545	711	343	445	82	267	256	80	76
C	878	944	632	632	360	113	272	538	132	198
D	1662	776	1080	590	698	171	399	404	266	109

*pre=before first dose of chemotherapy, post=4 months post chemotherapy

These preliminary data indicate that BP is a very effective and well tolerated chemotherapy regimen in patients with relapsed follicular lymphoma who have been previously received rituximab therapy. Our data also suggest that, in some patients, BP can cause a lymphopenia of variable intensity that may not fully recover four months after the last chemotherapy cycle. Studies of idiotype vaccine-induced humoral and cellular immune responses and their correlation with the presence of lymphopenia are ongoing. Updated results will be available at the time of the meeting.

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