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Abstract 3657 Short Course of Bendamustine and Rituximab Followed by 90Y-Ibritumomab Tiuxetan in Patients with Chemotherapy-Naïve Follicular Lymphoma: Early Results of "Fol-Brite"

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Background:

Bendamustine and rituximab is proving to be a superior first-line option in the treatment of follicular lymphoma. 90Y-ibritumomab tiuxetan is an effective consolidation strategy after chemotherapy induction in patients with follicular lymphoma, but has never been sequentially combined with bendamustine. In this prospective, single-arm, open-label, multicenter phase II trial (Fol-BRITE), we aim to assess the response rate and safety of a short induction course of bendamustine and rituximab (B-R) for 4 cycles followed by consolidation with 90Y-ibritumumab tiuxetan (90Y-IT) for chemotherapy-naïve patients with follicular lymphoma.

Methods:

Subjects greater than the age of 18 with chemotherapy-naïve follicular lymphoma (grade 1-2 and 3a) requiring treatment are eligible for this study. Treatment consists of an initial dose of rituximab 375mg/m2, and then one week later, bendamustine 90mg/m2 on days 1 and 2, and rituximab 375mg/m2 on day 1 of a 28-day cycle. B-R is given for a total of 4 cycles. Patients are eligible for consolidation with 90Y-IT if they obtain at least a partial response (PR) after induction, with a platelet count over 150,000/mm3, and granulocyte counts 1,500/mm3 and a bone marrow infiltration of <25%. The primary endpoint of this study is the determination of the complete response (CR) rate after sequential therapy with B-R followed by 90Y-IT. Secondary endpoints are overall response (OR=CR+PR) rate after a short course of B-R (4 cycles) and conversion rate from PR after B-R to CR after

90Y-IT. Secondary endpoints also include progression-free survival and safety. An optimal Simon two-stage design is incorporated to allow an early futility look for complete responses.

Results:

Nineteen patients have started treatment in this study to date, 13 have completed B-R and 7 have received 90Y-IT.

Response rates after 4 cycles of B-R: Thirteen patients have completed 4 cycles of B-R and 13 are evaluable for response. Seven of 13 evaluable patients have had a CR (53.8%) and 5 of 13 patients have had a PR (38.5%) after 4 cycles of B-R for an OR rate of 92.3%.

Response rates after B-R followed by 90Y-IT: Seven of 13 B-R-treated patients have received 90Y-IT and are evaluable for the primary endpoint of complete response. Of the 13 B-R treated patients, one patient in CR was unable to receive 90Y-IT due to thrombocytopenia, and one other patient was not eligible to receive 90Y-IT due to achievement of stable disease only. Six of the 7 evaluable patients are in CR (85.7%) and one patient remains in a PR (14.3%) after consolidation with 90Y-IT. Of the 3 subjects who attained a PR after B-R, 2 (66.7%) converted to a CR after 90Y-IT, with one late conversion 16 months after 90Y-IT.

Hematologic toxicities after B-R included grade 4 neutropenia (1), grade 3-4 lymphopenia (3), and no grade 3-4 thrombocytopenia, out of 13 patients evaluable. Hematologic toxicities after 90Y-IT were acceptable, including grade 3-4 neutropenia (6), grade 3-4 lymphopenia (5), and grade 3-4 thrombocytopenia (4), out of 7 patients evaluable for toxicity. There have been no incidences of neutropenic fever. All patients have recovered their blood counts 7 to 12 weeks after Y90-IT. One out of 19 patients treated in this study has developed chronic myelogenous leukemia, occurring 11 months after treatment with Y90-IT.

Conclusions:

In this early pre-planned analysis of the first-stage of an optimal Simon two-stage design, we report this combination of therapy is both effective and safe. The CR rate of patients completing all study therapy is 85.7%, and well exceeds the limits required to continue this trial with an accrual goal of 39 subjects. Sequential treatment with B-R followed by Y90-IT is a promising option for the treatment of follicular lymphoma.

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