

Pralatrexate Injection (Folotyn)

On September 24, 2009, the Office of Oncology Drug Products granted accelerated approval to pralatrexate injection (FOLOTYN, Allos Therapeutics, Inc.) for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL). This approval was based on an overall objective response rate observed in a single-arm trial. As a condition of the accelerated approval, randomized, controlled trials are required post-approval to verify and describe the clinical benefit of pralatrexate in PTCL.

Trial PDX 008 was an open-label, multicenter, international trial that enrolled 115 patients with PTCL who had relapsed or had progressive disease following prior therapy. The median number of prior systemic therapies was 3 (range 1 to 12). Twenty-four percent of patients did not have an objective response to any previous therapies; 63% did not have an objective response to the most recent prior therapy.

One hundred and nine evaluable patients received pralatrexate at a starting dose of 30 mg/m² administered as an intravenous push over 3-5 minutes once weekly for 6 weeks followed by a 1 week break (one cycle). In addition, each patient received vitamin B12, (1.0 mg IM) every 8-10 weeks and a daily administration of folic acid (1.0 - 1.25 mg orally). Imaging scans to assess disease status were performed at week 7 (end of cycle 1) and subsequently at 14 week intervals. Patients who had tumor responses or stable disease continued to receive additional cycles until disease progression or unacceptable toxicity.

Responses were assessed by an independent central imaging review committee using the International Workshop Criteria (IWC) for malignant lymphoma. The overall response rate (complete response plus complete response unconfirmed plus partial response) was 27% (95% CI: 19%, 36%). The median response duration was 9.4 months (range: 1-503 days). Thirteen patients (12% of 109 evaluable patients) had response durations \geq 14 weeks; the median response duration of these patients has not yet been reached (range: 98 to 503 days). Six of these 13 patients achieved complete responses, 1 patient had a complete response unconfirmed, and the remaining 6 patients had partial responses.

Safety assessments were performed on the 111 patients who received at least 1 pralatrexate dose. Mucositis, thrombocytopenia, nausea, fatigue, anemia, constipation, pyrexia, edema, cough, epistaxis, vomiting, neutropenia, and diarrhea were the most common adverse reactions. Adverse reactions were the reason for dose reductions in 31% of patients, dose omission in 69%, and treatment withdrawal in 23%. Overall, 85% of scheduled doses were administered.

Serious adverse events were reported in 44% of patients. The most common serious adverse events (reported in \geq 3 patients) were pyrexia, mucositis, febrile neutropenia, sepsis, and thrombocytopenia. Eight deaths were reported within 30 days of the last pralatrexate dose. Seven were attributed to progressive disease and one was due to cardiopulmonary arrest possibly related to pralatrexate.

Full prescribing information, including clinical trial information, safety, dosing, drug-drug interactions and contraindications is available at

http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/022468lbl.pdf

