Elotuzumab, First-in-Class Monoclonal Antibody Immunotherapy, Improves Outcomes in Patients with Multiple Myeloma

By Phoebe Starr

The addition of the novel monoclonal antibody elotuzumab to dexamethasone plus lenalidomide resulted in a 30% reduction in the risk for disease progression and death in patients with relapsed or refractory multiple myeloma.

These interim results of a landmark ELOQUENT-2 phase 3 trial, which were presented at ASCO 2015, represent the largest study of a monoclonal antibody in multiple myeloma and the first positive findings for a targeted immunotherapy approach in a phase 3 clinical trial in patients with multiple myeloma. Further studies of elotuzumab are ongoing in myeloma, and the drug has received a breakthrough therapy designation from the US Food and Drug Administration for patients who have received ≥1 previous therapies for multiple myeloma.

"We are excited about the progression-free survival [PFS] results attributable to this novel first-in-class monoclonal antibody. Elotuzumab achieved a longer duration of remission and improved overall response rates, without a significant increase in adverse events and no reduction in quality of life," said lead investigator Sagar Lonial, MD, Chief Medical Officer, Winship Cancer Institute, Emory University School of Medicine, Atlanta. "We hope elotuzumab will be the first immune approach to be added to the management of relapsed/refractory multiple myeloma."

Dr Lonial explained that elotuzumab's novel mechanism of action contains a "double whammy," by attaching to a cell-surface protein called SLAMF7 (signaling lymphocytic activation molecule F7), which is found on multiple myeloma cells and natural killer cells. "Thus, it acts directly on the tumor itself, and enhances the activity of natural killer cells to kill the tumor," he said.

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ELOQUENT-2 Phase 3 Trial

The study randomized 646 patients with relapsed or refractory multiple myeloma to standard therapy with lenalidomide and dexamethasone or to standard therapy plus elotuzumab. All patients had disease refractory to 1 to 3 previous therapies.

"These patients enrolled in the trial early in the treatment phase. They had failed initial therapies but not multiple therapies, so they do not represent end-stage truly refractory patients," Dr Lonial said.

At a median follow-up of 24 months, the PFS rates were 41% in the triple-therapy arm and 27% in the standard-therapy arm (P = .004). At 1 year, the PFS rates were 68% and 57%, respectively.

The overall response rates were 79% and 66% (P = .002), respectively, representing an absolute difference of 13% at 24 months.

"It is striking that 2 curves for each treatment arm remain separated at 2 years, which speaks to the duration of response and the power of an immune approach as part of treatment of multiple myeloma," Dr Lonial said.

Of note, patients at high risk as a result of the 19p deletion or t(4;14) genetic abnormalities had a similar benefit from elotuzumab as patients with average risk. These patients typically have less benefit from conventional therapies, Dr Lonial noted.

Overall, elotuzumab was well-tolerated, with no significant increases in adverse events. Approximately 10% of the patients had a mild infusion reaction with the first few doses of the monoclonal antibody immunotherapy.

"This therapy is an innovative approach, one that combines the precision of a targeted, immune-based therapy with traditional myeloma therapy. The results are very encouraging, giving renewed hope to patients who have relapsed," stated ASCO President-Elect Julie M. Vose, MD, MBA, Chief of the Division of Oncology/Hematology, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, who was not involved in this trial. ■

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FDA Expedites Approval of Lenvatinib...

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appetite, decreased weight, nausea, stomatitis, headache, vomiting, proteinuria, swelling and pain in the palms, palmar-plantar erythrodysesthesia syndrome, and dysphonia.

Lenvatinib is associated with serious side effects, including cardiac failure, arterial thromboembolic events, hepatotoxicity, renal failure and impairment, gastrointestinal perforation or fistula formation, QT interval prolongation, hypocalcemia, reversible posterior leukoencephalopathy syndrome, hemorrhage, risks to an unborn child, and impaired suppression of thyroid-stimulating hormone production. **(February 13, 2015)**

Lenalidomide plus Dexamethasone Receives Expanded Indication for Patients with Newly Diagnosed Myeloma

The FDA approved an expanded indication for lenalidomide (Revlimid; Celgene Corporation) in combination with dexamethasone for the treatment of patients with newly diagnosed multiple myeloma. This combination was previously approved for the treatment of patients with multiple myeloma who had received ≥1 therapies before.

The approval was based on the results of several phase 3 clinical trials, including the FIRST trial. This trial evaluated the continuous use of a regimen of lenalidomide plus dexamethasone (Rd) until disease progression compared with the regimen of melphalan, prednisone, and thalidomide (MPT) for 18 months as the primary analysis; a secondary analysis evaluated the use of Rd at a fixed duration of 18 cycles in 1623 patients with newly diagnosed myeloma who were not candidates for stem-cell transplant.

The primary end point in this randomized, open-label, 3-arm trial was median progression-free survival (PFS). The PFS was significantly longer among patients who received the continuous Rd regimen

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