By Devon Schuyler

Daratumumab Improves Progression-Free Survival in Relapsed/Refractory Myeloma

The addition of daratumumab (Darzalex, Janssen) to standard backbone regimens improved survival in patients with relapsed or refractory multiple myeloma, according to the results of two phase 3 trials published in the October 6 issue of the *New England Journal of Medicine*. Daratumumab increased the risk of neutropenia and infusion-related reactions but had a "reasonable" side effect profile, according to an editorial by Drs S. Vincent Rajkumar and Robert Kyle that accompanied the articles.

In the first trial, called CASTOR, Dr Antonio Palumbo and colleagues randomly assigned 498 patients with relapsed or refractory multiple myeloma to receive bortezomib and dexamethasone either alone (the control group) or in combination with daratumumab (the daratumumab group).

The rate of progression-free survival (PFS) at 12 months was significantly higher in the daratumumab group than in the control group, at 60.7% vs 26.9%. The rate of overall response after a median of 7.4 months also was significantly higher in the daratumumab group than in the control group, at 82.9% vs 63.2%. Infusion-related reactions and grade 3 or 4 thrombocytopenia and neutropenia were more frequent in the daratumumab group than in the control group.

In the second trial, called POLLUX, Dr Meletios A. Dimopoulos and colleagues randomly assigned 569 patients with relapsed or refractory multiple myeloma to receive lenalidomide (Revlimid, Celgene) and dexamethasone either alone (the control group) or in combination with daratumumab (the daratumumab group).

The rate of PFS at 12 months was significantly higher in the daratumumab group than in the control group, at 83.2% vs 60.1%. The rate of overall response after a median of 13.5 months also was significantly higher in the daratumumab group than in the control group, at 92.9% vs 76.4%. Infusion-related reactions and grade 3 or 4 neutropenia were more frequent in the daratumumab group than in the control group.

The editorialists concluded that based on these and other studies, daratumumab with lenalidomide and dexamethasone is the "clear standout" for patients with relapsed or refractory multiple myeloma, and daratumumab with bortezomib and dexamethasone is a "major option" for those whose disease is refractory to lenalidomide. Another "reasonable alternative" is the older regimen of bortezomib, cyclophosphamide, and dexamethasone.

Although daratumumab represents a "landmark advance" in the treatment of myeloma, the editorialists cautioned against its use in situations where it has not been shown to improve outcomes.

More Evidence for Better Prognosis With Left-Sided Metastatic Colorectal Cancer

Patients with metastatic colorectal cancer whose tumors were on the left side had a significantly better prognosis than those whose tumors were on the right side, according to an analysis of 2 studies in patients with *RAS* wild-type tumors. The finding is consistent with those of other recent studies.

For the study, which appeared online October 10 in *JAMA Oncology*, Dr Sabine Tejpar and colleagues conducted a retrospective analysis of 175 patients from the CRYSTAL trial and 195 patients from the FIRE-3 trial who had *RAS* wild-type metastatic colorectal cancer. Approximately three-quarters of the patients had left-sided tumors.

The researchers found that patients with left-sided tumors had better PFS and overall survival (OS) and a better objective response rate than those with right-sided tumors. In addition, the use of the epidermal growth factor receptor (EGFR) inhibitor cetuximab (Erbitux, Lilly) most benefitted patients with left-sided tumors.

In the CRYSTAL study, patients with left-sided tumors did not have significantly better OS than those with right-sided tumors if they received chemotherapy alone (21.7 vs 15.0 months; hazard ratio [HR], 1.35; P=.11). By contrast, patients with left-sided tumors had significantly better OS than those with right-sided tumors if they received chemotherapy plus cetuximab (28.7 vs 18.5 months; HR, 1.93; P=.003). In the FIRE-3 study, OS for patients with left-sided tumors was significantly better among those who received chemotherapy plus cetuximab than among those who received chemotherapy plus bevacizumab (Avastin, Genentech; 38.3 vs 28.0 months; HR, 0.63; P=.009). OS for patients with right-sided tumors was not significantly better for those who received chemotherapy plus cetuximab than for those who received chemotherapy plus bevacizumab (18.3 vs 23.0 months; HR, 1.31; P=.28).

The authors concluded that "primary tumor location should be included in the stratification criteria" for future trials of metastatic colorectal cancer, especially those examining the use of EGFR inhibitors.