

Cyclophosphamide, Lenalidomide, and Dexamethasone Improve Survival in Multiple Myeloma

In the April 25 issue of the *American Journal of Hematology*, Kumar and colleagues reported the results of a phase II trial that investigated the combination of cyclophosphamide, lenalidomide (Revlimid, Celgene), and dexamethasone as initial therapy for multiple myeloma. A total of 53 patients with previously untreated multiple myeloma received 4-week cycles of lenalidomide (25 mg/day for 3 weeks), dexamethasone (40 mg weekly), and cyclophosphamide (300 mg/m² weekly for 3 weeks). Following treatment, a partial response or better was observed in 85% of patients, among whom 47% exhibited a very good partial response or better. The median progression-free survival (PFS) was 28 months (95% confidence interval [CI], 22.7–32.6 months). Overall survival (OS) at 2 years was 87% (95% CI, 78–96%). There was no significant difference in PFS or OS for patients with high-risk multiple myeloma (n=14) versus the standard-risk patients (n=39). Toxicities were manageable, and more than 80% of the planned doses were administered. There were 6 patients who discontinued the study due to toxicities. The study investigators concluded that the combination of cyclophosphamide, lenalidomide, and dexamethasone is well tolerated and an effective regimen for upfront and long-term treatment of multiple myeloma.

Long-Term Results of the BA06 30894 Trial

The long-term study results of the BA06 30894 trial, which assessed the use of neoadjuvant cisplatin, methotrexate, and vinblastine (CMV) chemotherapy in patients with muscle-invasive urothelial cancer of the bladder treated by cystectomy and/or radiotherapy, were published on April 18 in the advanced online issue of the *Journal of Clinical Oncology*. Between 1989 and 1995, 976 patients were recruited and randomized to receive either 3 cycles of CMV chemotherapy or no neoadjuvant chemotherapy. The median follow-up is currently 8 years. The results showed a significant reduction in the risk of death after CMV treatment (hazard ratio [HR], 0.84; 95% CI, 0.72–0.99; *P*=.037, corresponding to an increase in 10-year survival from 30% to 36%). Griffiths and associates concluded that for invasive bladder cancer

patients, CMV chemotherapy as first-line adjunctive treatment improves outcome. They support the use of neoadjuvant chemotherapy followed by definitive local therapy over cystectomy or radiotherapy alone in treating patients with deeply invasive bladder cancer.

New Biomarkers for EGFR Inhibition Identified: Updated BATTLE Trial Results

The updated results of the BATTLE (Biomarker-integrated Approaches of Targeted Therapy for Lung Cancer Elimination) trial were presented in April at the 102nd annual meeting of the American Association for Cancer Research (AACR). Heymach and coworkers analyzed core needle biopsies to perform gene expression profiling on 101 patients in the BATTLE trial. The presence of a novel 5-gene signature was predictive of response to erlotinib (Tarceva, Genentech/Osi Oncology), including among patients with wild-type epidermal growth factor receptor (EGFR). The 5 genes are *LCN2*, *NPR3*, *OGG1*, *TRIM72*, and *C5orf23*. After 8 weeks, the disease was controlled in 83% of patients with the gene signature compared to none of the patients without the signature. Lipocalin-2, a protein encoded by the *LCN2* gene, is a promising potential target for therapy, as it is involved in the EGFR pathway. Investigators found that the presence of an epithelial-to-mesenchymal signature also predicted disease control. Disease control at 8 weeks was achieved in 64% of patients whose cells were still epithelial type; only 10% of those with mesenchymal-type cells achieved disease control. An additional potential therapeutic target is the *Axl* gene, which is associated with mesenchymal-type cells. The predictive value of both sets of gene signatures—as well as markers from the PI3K-AKT pathway, EGFR signatures, and *KRAS* mutations—will be prospectively tested in the upcoming BATTLE 2 trial. The researchers aim to determine which patients will respond to EGFR inhibition with erlotinib, especially among those who do not have an EGFR mutation.

Improved Outcomes With Low-Dose Decitabine Over Best Supportive Care in Elderly Patients With Intermediate- or High-Risk MDS

According to the final results of the randomized, phase III study of the European Organisation for Research and Treatment of Cancer Leukemia Group and the

German MDS Study Group, low-dose decitabine is active in older, higher-risk myelodysplastic syndrome (MDS) patients, in whom it improves survival and quality of life. In this study by Lübbert and colleagues, 233 patients with a median age of 70 years (range 60–90 years) were enrolled. At randomization, the median duration of MDS was 3 months; 53% of patients had poor-risk cytogenetics. The primary endpoint was OS. Decitabine (15 mg/m²) was administered intravenously over 4 hours 3 times a day for 3 days in 6-week cycles. No statistical significance in OS prolongation was observed in patients treated with decitabine versus best supportive care (median OS, 10.1 vs 8.5 months, respectively; HR, 0.88; 95% CI, 0.66–1.17 months; 2-sided, log-rank $P=.38$). Decitabine significantly prolonged PFS (6.6 vs 3.0 months, respectively; HR, 0.68; 95% CI, 0.52–0.88 months; $P=.004$) but not acute myeloid leukemia (AML)–free survival (8.8 vs 6.1 months, respectively; HR, 0.85; 95% CI, 0.64–1.12 months; $P=.24$). There was a significant reduction in AML transformation at 1 year, from 33% with best supportive care to 22% with

decitabine ($P=.036$). Worse outcomes were observed in patients with short MDS duration, according to multivariate analyses.

In the decitabine cohort, 13% of patients achieved a complete response and 6% achieved a partial response. No patients in the best supportive care cohort achieved these outcomes. Patients in the best supportive care group were more likely to experience stable disease (22% vs 14%). Other outcomes included hematologic improvement (15% in the decitabine cohort vs 2% in the best supportive care group), progressive disease (29% vs 68%, respectively), and hypoplasia (14% vs 0%, respectively). In each cohort, 8% of patients were inevaluable. Grade 3/4 infections were reported in 57% of decitabine patients and 52% of best supportive care patients. Grade 3/4 febrile neutropenia occurred in 25% of patients treated with decitabine versus 7% of patients who received best supportive care. Decitabine patients experienced improvements in quality of life parameters. These final results were published in the April 14 issue of the *Journal of Clinical Oncology*.