HEM/ONC News

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Gefitinib Doubles Progression-free Survival (PFS) in Patients With Non–small-cell Lung Cancer (NSCLC) With Mutated Epidermal Growth Factor Receptor (EGFR)

A phase III study conducted in Japan reported in the June 24 issue of the *New England Journal of Medicine* found that compared to standard chemotherapy with paclitaxel and carboplatin, gefitinib (Iressa, AstraZeneca) doubled PFS in patients with EGFR-mutated NSCLC. The study, which was conducted by the North-East Japan Study Group, randomized 230 patients to either gefitinib (250 mg/day) or intravenous paclitaxel (200 mg/m^2) and carboplatin (area under the concentration curve 6) as first-line treatment. The patients enrolled in the study had stage IIB or IV NSCLC or postoperative relapse. Chemotherapy was administered for a minimum of 3 cycles and was given on the first day of every 3-week cycle; gefitinib was given until disease progression, intolerable toxicity, or withdrawal of consent. The primary endpoint was PFS and the secondary endpoints were overall survival, response rate, and toxicity. The study was started in March 2006 but closed early in May 2009 after a significant benefit in PFS was seen in the gefitinib group. The interim analysis of the first 200 patients showed a median PFS of 10.4 months in patients receiving gefitinib and 5.5 months in those receiving chemotherapy. The PFS benefit was also seen in the final analysis (10.8 months for gefitinib vs 5.4 months for chemotherapy). The response rates were also significantly higher in the patients receiving gefitinib compared to those receiving chemotherapy (73.7% vs 30.7%), though overall survival did not differ significantly. The safety evaluation found that hematologic adverse events and neurotoxicity were more common in those receiving chemotherapy. Furthermore, severe adverse events were more frequently observed in the chemotherapy group (71.7% vs 41.2%). The study findings support the use of gefitinib as first-line therapy in patients with EGFR-mutated metastatic NSCLC.

Higher Rates of Response Seen With Nilotinib Compared to Imatinib in Patients With Newly Diagnosed Chronic Myeloid Leukemia

In the June 4 issue of the *New England Journal of Medicine*, investigators reported results of the ENESTnd (Evaluating Nilotinib Efficacy and Safety in Clinical Trials-Newly Diagnosed Patients) trial—a randomized, open-label, phase III trial comparing nilotinib (Tasigna, Novartis) to imatinib (Gleevec, Novartis) in patients with chronic-phase chronic myeloid leukemia (CML). The study enrolled 846 adult patients with an Eastern Cooperative Oncology Group performance status of 0–2 who were randomized 1:1:1 to nilotinib 300 mg twice daily (n=282), nilotinib 400 mg twice daily (n=281), or imatinib 400 mg once daily n=283). Patients were treated until failure or occurrence of unacceptable toxicity. Major molecular response (mMR) was evaluated at baseline, every month for 3 months, and then every 3 months. mMR within 24 months and complete cytogenetic response (cCR) within 12 months were also evaluated. The median duration of treatment was 14 months. At 12 months, the rate of mMR was significantly higher in those receiving 300 mg and 400 mg nilotinib compared to those receiving imatinib (44% and 43% vs 22%). The median time to mMR was shorter in the nilotinib groups compared to the imatinib group (8.6 and 11 months vs not reached). The rate of cCR at 12 months was also significantly higher in the nilotinib groups compared to the imatinib group. The safety evaluation demonstrated that both drugs were reasonably well tolerated; grade 3/4 neutropenia and anemia were most common in the imatinib group, whereas grade 3/4 thrombocytopenia were more common in the nilotinib groups. Although the study results showed that nilotinib had significantly higher rates of mMR and cCR in newly diagnosed CML, further studies are needed.

In Brief

Data from the EACH (Phase III Study of FOLFOX4 vs Doxorubicin in Asian Patients With Advanced Hepatocellular Carcinoma) trial showed that 5-fluouracil, leucovorin, and oxaliplatin (FOLFOX4) significantly increased median time to progression compared to doxorubicin in Asian patients with advanced hepatocellular carcinoma. *(J Clin Oncol. 2010;28:15s. Abstract 4008.)*

The addition of cetuximab to frontline oxaliplatin-based chemotherapy did not improve overall survival or PFS in KRAS wild-type patients with metastatic colorectal cancer, according to the investigators of the randomized phase III COIN (Combination Chemotherapy With or Without Cetuximab as First-Line Therapy in Treating Patients With Metastatic Colorectal Cancer) trial. *(J Clin Oncol. 2010;28:15s. Abstract 3502.)*