

First-line Lapatinib is Safe and Effective for ErbB2-amplified Breast Cancer

The results of a multi-institution study evaluating the efficacy and tolerability of two dosing schedules of lapatinib (Tykerb, GlaxoSmithKline) as first-line monotherapy in women with ErbB2-amplified locally advanced or metastatic breast cancer were published in the June 20 issue of the *Journal of Clinical Oncology*. One hundred thirty-eight women who were previously untreated in the metastatic setting were randomly assigned to receive either 1,500 mg once daily (n=69) or 500 mg twice daily (n=69) of lapatinib. Clinical response was evaluated by radiologic assessments at weeks 8 and 12 and every 12 weeks thereafter. Patients were treated for a median of 17.6 weeks. In the intent-to-treat population, the overall response (OR) rate (complete response [CR] plus partial response [PR]) was 24%; there was no significant difference in the OR between the two lapatinib groups ($P=.691$). The median time to response was 7.9 weeks and the median duration of response was 28.4 weeks. The progression-free survival (PFS) rates for the 1,500 mg daily group and the 500 mg twice-daily group at 4 and 6 months were 60% and 67% and 41% and 45%, respectively. The median time to treatment failure was 16.1 weeks. The most common adverse events (AEs) were diarrhea and rash; both were grade 1 or 2. Nineteen patients experienced grade 3 AEs and 6 patients reported grade 4 AEs. The most common AEs related to lapatinib treatment were grade 1 and 2 diarrhea, rash, pruritis, and nausea. Serious AEs were noted in 33 patients and 9 patients reported serious adverse reactions related to treatment. Seven patients withdrew from the study due to treatment-related AEs and 6 patients died during the study. Overall, there was no significant difference in efficacy or safety between the two dosing schedules. Study findings confirmed that lapatinib demonstrated clinical activity as either 1,500 mg administered once daily or 500 mg administered twice daily.

Pegylated Liposomal Doxorubicin Beneficial in Hard-to-treat Cutaneous T-cell Lymphoma

Earlier studies of pegylated liposomal doxorubicin (Doxil, Ortho Biotech) have found it to be efficacious and associated with a low rate of AEs. Recent study findings, reported in the June issue of the *Archives of Dermatology*, confirmed that pegylated liposomal doxorubicin is clinically beneficial in advanced or refractory cutaneous T-cell lymphoma (CTCL). The study, led by Dr. Brigitte Dreno, which was conducted at 13 sites in France, included patients with either stage II–IV CTCL who failed at least two lines of previous treatment or who had histologically transformed epidermotropic CTCL that

required chemotherapy. Patients (n=25) were administered intravenous pegylated liposomal doxorubicin (40 mg/m²) once every 4 weeks; this dose represents a higher dose than was previously tested. The primary endpoint of objective response was noted in 14 of 25 (56%) patients; 5 patients experienced CR and 9 patients experienced PR. The median OS was 43.7 months and the median PFS after treatment completion was 5 months. Of note, responses were observed in two subsets of patients with known poor prognosis: patients with Sézary syndrome (OR, 60%) and patients with transformed CTCL (OR, 50%). Study results found that dose escalation did not improve efficacy but, rather, increased toxicities, particularly hematologic toxicities, compared to the previously studied dose of 20 mg/m².

Imatinib for Newly Diagnosed Patients With Chronic-phase Chronic Myeloid Leukemia

Imatinib (Gleevec, Novartis) is very effective in treating newly diagnosed patients with chronic myeloid leukemia (CML) in chronic phase (CP). Currently, the available supportive data are based on results from a single multi-institution study (IRIS). A recent study, published in the July 10 issue of the *Journal of Clinical Oncology*, enrolled 204 patients with *BCR-ABL*-positive CML in CP who received imatinib (400 mg daily) as first-line therapy from 2000 to 2006. Imatinib was started within 6 months of diagnosis and dose was adjusted according to tolerance and response. The patients had not received any prior treatment for leukemia other than hydroxyurea. The study evaluated hematologic, cytogenetic, and molecular response and survival (PFS, OS, and event-free survival). At 5 years, the cumulative incidences of complete hematologic response (CHR), complete cytogenetic response (CCyR), and major molecular response were 98.5%, 82.7% and 50.1%, respectively. OS and PFS were 83.2% and 82.7%, respectively. It was noted that patients who achieved CCyR at 1 year had a better PFS and OS than those who did not reach CCyR. By 5 years, 25% of patients discontinued treatment because of bad response and/or toxicity. Patient samples were also analyzed for kinase domain (KD) mutations to determine any resistance to imatinib. The development of these mutations was a predictor for loss of CCyR, but not for loss of CHR, PFS, or OS. At 5 years, the cumulative incidence of KD mutations was 8.6%. The researchers concluded that imatinib is very effective in most patients with CP CML and that patients who respond to therapy are likely to live substantially longer. However, many patients do not respond or become resistant to imatinib, and for these patients, there is a need for better therapy.