

First-line Nilotinib and Dasatinib Sustain Advantages Over Imatinib

Updates from pivotal phase III trials of the second-generation tyrosine kinase inhibitors dasatinib (Sprycel, Bristol-Myers Squibb) and nilotinib (Tasigna, Novartis) showed that these agents maintained their separate advantages over imatinib (Gleevec, Novartis) in treating chronic myeloid leukemia (CML). At the 2010 American Society of Hematology (ASH) meeting, Hughes presented 2-year follow-up data from the ENESTnd (Evaluating Nilotinib Efficacy and Safety in Clinical Trials-Newly Diagnosed Patients) trial, which compared 300 mg nilotinib twice daily (n=282), 400 mg nilotinib twice daily (n=281), and 400 mg imatinib once daily (n=283). Durable major molecular response was as follows: 300-mg nilotinib group, 62%; 400-mg nilotinib group, 59%; imatinib group, 37% ($P<.001$). Durable responses were observed in all 3 arms, with less than 2% of patients losing response between 12 and 24 months. Complete cytogenetic response (CCyR) rates remained significantly different at 87% in the 300-mg nilotinib arm and 85% in the 400-mg nilotinib arm, versus 75% in the imatinib arm. The imatinib arm had higher treatment failure rates, more patients who progressed to accelerated or blast phase, and more CML-related deaths than the nilotinib arms. Also at the 2010 ASH meeting, Dr. Shah presented 18-month follow-up data on the DASISION (Dasatinib versus Imatinib Study in Treatment-Naive CML Patients) trial, which compared 100 mg/day of dasatinib to 400 mg/day of imatinib in 2 cohorts of 258 patients each. CCyR rates were 78% and 70%, respectively ($P=.0366$). More imatinib patients progressed to accelerated or blast-phase CML (9 vs 6, respectively). Death occurred more frequently in the dasatinib arm (11 vs 6) but was not drug-related.

Tumor Control Improvement With Escalated BEACOPP in Unfavorable HL

According to the final analysis of the German Hodgkin Study Group (GHSG) HD14 trial, the overall survival and freedom from treatment failure at 5 years for Hodgkin lymphoma (HL) patients in unfavorable stages treated with escalated-dose bleomycin, etoposide, adriamycin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPP) and adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD) plus radiotherapy (RT) was 94.3%, compared with 87.6% for those treated with ABVD/RT alone. Patients in arm A (n=818) received 4 cycles of ABVD, and patients in arm B (n=805) received 2 cycles of BEACOPP escalated

followed by 2 cycles of ABVD. All patients received 30 Gy of involved-field radiation therapy (IFRT). At a median follow-up of 42.4 months, there were 20 deaths in each arm, and 19 patients in arm A versus 16 patients in arm B had secondary neoplasia. Progressive disease and early relapse rates were observed in 2.9% and 2.8% of patients in arm A, compared with 0.9% and 0.9% of patients in arm B, respectively. Although acute grade 3/4 toxicity rates of chemotherapy were higher in arm B (87.1%) than in arm A (50.7%), no differences in treatment-related death or secondary neoplasia were found between the study arms. Borchmann and associates reported the final analysis of the GHSG HD14 trial at the 2010 ASH meeting. They concluded that there is a significant improvement in tumor control for patients with early unfavorable HL when treatment is intensified using 2 cycles of escalated-dose BEACOPP followed by 2 cycles of ABVD and IFRT compared to the prior standard of 4 cycles of ABVD plus IFRT.

Circulating Tumor Cells Help Predict Recurrence and Death in Breast Cancer

At the 2010 San Antonio Breast Cancer Symposium, Rack and colleagues reported on a subset analysis of patients from the 251-center German SUCCESS (Simultaneous Study of Docetaxel-Gemcitabine Combination Adjuvant Treatment, as well as Extended Bisphosphonate and Surveillance Trial) study examining the use of serial blood sampling for circulating tumor cells (CTCs). In this phase III, randomized trial, peripheral blood samples of 23 mL were analyzed from 307 N-positive and high-risk N-negative postmenopausal patients with hormone-sensitive breast cancer. Patients had received adjuvant taxane-based chemotherapy 2 years before study entry and were currently undergoing treatment with tamoxifen or anastrozole. The CellSearch system (Veridex) was used to detect the presence of CTCs. Before the start of adjuvant treatment, 21.5% of patients had 1 or more CTCs in their blood; these patients were more frequently node-positive, but other links to tumor size, grade, or HER2 status were not apparent. Recurrence of breast cancer was evident in 144 patients, and death occurred in 66 patients. CTC positivity proved to be a significant independent predictor for disease-free and overall survival. The increased risk of early breast cancer recurrence was 88% for patients with 1 to 4 CTCs versus 400% for patients with at least 5 CTCs. Patients with 1 to 4 CTCs experienced a 91% increased risk of death compared to a 300% increased risk for those with 5 or more CTCs.