EORTC led intergroup trial investigates Imatinib failure-free survival in patients with GIST

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Interim results of an EORTC intergroup trial have confirmed that adjuvant imatinib impacts short-term freedom from relapse in patients with localized, surgically resected, high/ intermediate-risk GIST. In the high-risk subgroup, a non-statistically significant trend in favor of the adjuvant arm was observed in terms of Imatinib failure-free survival. This new endpoint for the adjuvant setting, survival free from any failure of the first employed tyrosine kinase inhibitor, was designed to incorporate secondary resistance, currently the main factor adversely affecting prognosis of patients with advanced GIST.

Standard treatment for patients with gastrointestinal stromal tumors (GIST), sarcomas of the gastrointestinal wall, is surgery. Neither chemotherapy nor radiation therapy work well for these patients, but EORTC trials had shown that a targeted therapy, the tyrosine kinase inhibitor Imatinib (known as Glivec in Europe and GleevecTM in the US), is effective in treating patients with advanced GIST. The intergroup randomized controlled phase III EORTC 62024 trial, then, took the logical next step of determining whether Imatinib would also be effective as an adjuvant to surgery in patients with local disease.

Originally, the primary endpoint for this trial was overall survival; relapse-free survival, relapse-free interval, and toxicity were secondary endpoints. In 2009, however, the Independent Data Monitoring Committee, noting the prognostic improvement of patients with

advanced GIST, authorized a change in the primary endpoint to Imatinib failure-free survival. Imatinib failure was defined as the time when treatment with a different tyrosine kinase inhibitor began.

The results of EORTC trial 62024 will be presented Monday, 03 June 2013 at an ASCO 2013 Oral Abstract Session by Dr. Paolo Giovanni Casali of the Fondazione IRCCS Istituto Nazionale dei Tumori in Milan and Coordinator of this study.

Between 2005 and 2008, 908 patients with localized, surgically resected, high/intermediate-risk GIST were randomized to Imatinib (400 mg Imatinib daily, 454 patients) or observational (no further therapy after surgery, 454 patients) treatment arms. A total of 835 patients were eligible.

This planned interim analysis was conducted after the occurrence of 115 events according to the Imatinib failure-free survival primary end-point with a significance level of 1.5%. At a median follow-up of 4.7 years, the 5-year Imatinib failure-free survival was 87% in the Imatinib arm and 84% in the observational arm (HR=0.80, 98.5% CI [0.51; 1.26], p=0.23). At three years, relapse-free survival was 84% in the Imatinib arm and 66% in the observational arm, while at five years relapse-free survival was 69% in the Imatinib arm and 63% in the observational arm (p