595 The EUTOS Survival Score Is Preferable over the Sokal Score for Prognosis of Long-Term Survival of Patients with Chronic Myeloid Leukemia

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Introduction: The in-study and out-study sections of the European Treatment and Outcome Study (EUTOS) registry comprise data on imatinib-treated adult patients with chronic myeloid leukemia (CML) who were prospectively enrolled in clinical studies or registries between 2002 and 2006. All patients diagnosed with chronic-phase Philadelphia chromosome-positive CML were eligible for analysis. The new EUTOS long-term survival (ELTS) score was developed in 2,205 in-study patients (Blood 2014; 124(21):153). Its purpose is the discrimination of three risk groups with clinically significantly different probabilities of dying from CML. The score was validated in 1,120 out-study patients.

Aims: Up to now, many investigators still apply the Sokal score for the prognostic discrimination of CML-patients treated with tyrosine kinase inhibitors (TKIs). The Sokal score allocated more than 20% of chronic-phase patients to the high-risk group while it was 12% with the new ELTS score. Long-term outcome with tyrosine kinase inhibitors (TKIs) suggests that the allocation of more than 20% chronic-phase CML patients into a high-risk group is too pessimistic. The focus of this analysis was the comparison of risk group allocations and prognosis between the two scores.

Methods: Survival time was calculated from the date of start of treatment to death or to the latest follow-up date. Survival was censored at the time of allogeneic stem cell transplantation in first chronic phase. Cumulative incidence probabilities (CIPs) of dying of CML were compared with the Gray test and overall survival probabilities with the log-rank test. As “death due to CML”, only death after confirmed disease progression was regarded. Progression was defined in accordance with the recommendations of the ELN (Baccarani et al, Blood 2013). Level of significance was 0.05.

Results: Both registries combined, the 3,325 patients had a median observation time of 6.1 years. Six-year overall survival probability was 91% (95% confidence interval (CI): 89-92%). Death was due to CML in 142 of 309 deceased patients (46%).The 6-year CIP of dying of CML was 4% (CI: 4-5%).

From low to high risk groups, the Sokal score resulted in 6-year CIPs of 3% (n=1358 (41%), CI: 2-4%), 4% (n=1209 (36%), CI: 3-5%), and 8% (n=758 (23%), CI: 6-11%) and the ELTS score in 6-year CIPs of 2% (n=2030 (61%), CI: 2-3%), 6% (n=898 (27%), CI: 4-7%), and 13% (n=397 (12%), CI: 10-17%).

Of the 758 patients allocated to high risk by the Sokal score, the ELTS score classified 165 (22%) as low risk and 265 (35%) as intermediate risk. Compared to the 328 high-risk patients (43%) according to both scores (6-year CIP of dying: 13%, CI: 9-17%), the CIPs of dying were significantly lower for the 165 low-risk patients (p=0.0062, 6-year CIP: 5%, CI: 2-9%) and for the 265 intermediate-risk patients (p=0.0050, 6-year CIP: 5%, CI: 3-9%). These 430 Sokal high but ELTS non-high-risk patients (6-year OS: 89%. CI: 86-92%) showed significantly higher OS probabilities than the 328 Sokal and ELTS high-risk patients (p=0.030, 6-year OS: 81%. CI: 76-85%).

Of the 2030 patients identified as low risk by the ELTS score, the Sokal score allocated 603 (30%) to the intermediate- and 165 (8%) to the high-risk group. Without significant CIP differences to the latter group, at 6 years, the CIP of dying was 2% (CI: 1-3%) in the 1262 low-risk and also 2% in the 603 intermediate-risk patients (CI: 1-3%). The OS probabilities of the 768 non-low-risk patients according to the Sokal score (6-year OS: 93%. CI: 91-95%) were not significantly different from the 1262 classified as low-risk by both scores (6-year OS: 95%. CI: 93-96%).

Conclusions: To be able to perform comparisons between the various prognostic groups suggested by the Sokal and the EUTOS survival score with a reasonable power, data of in- and out-study samples were combined. The Sokal score allocated an absolute difference of 12% (n=430) more patients to the high-risk groups than the EUTOS survival score. As these patients had significantly and clinically relevantly lower CIPs and higher OS probabilities, the allocation of the Sokal score was not appropriate. Contrarily, the long-term outcome of 768 patients assessed as low-risk by the ELTS and non-low-risk by the Sokal score was not different from the outcome of 1262 assesses as low-risk patients by both scores. For prognosis of long-term survival outcome, the use of the EUTOS survival score is recommended.

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