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Original Research

Survival trends in childhood chronic myeloid leukaemia in Southern-Eastern Europe and the United States of America

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Abstract ***Aim:*** To assess trends in survival and geographic disparities among children (0–14 years) with chronic myeloid leukaemia (CML) before and after the introduction of molecular therapy, namely tyrosine kinase inhibitors (TKIs) in Southern-Eastern European (SEE) countries and the USA.
Methods: We calculated survival among children with CML, acute lymphoblastic (ALL) and acute myeloid leukaemia (AML) in 14 SEE (1990–2014) cancer registries and the U.S. Surveillance, Epidemiology and End Results Program (SEER, 1990–2012). We used Kaplan–Meier curves and multivariate Cox regression models to calculate hazard ratios (HRs) with 95% confidence intervals (CIs).
Results: Among 369 CML cases, substantial improvements were noted in 2-year survival during the post-TKI (range: 81–89%) compared to pre-TKI period (49–66%; HR: 0.37, 95% CI: 0.23–0.60). Risk of death was three times higher for <5-year-old children versus those aged 10–14 years (HR: 3.03, 95% CI: 1.85–4.94) and 56% higher for those living in SEE versus SEER (HR: 1.56, 95% CI: 1.01–2.42). Regardless of geographic area and period of TKI administration, however, age seems to be a significant determinant of CML prognosis (pre-TKI period, HR_{0-4y}: 2.71, 95% CI: 1.53–4.79; post-TKI period, HR_{0-4y}: 3.38, 95% CI: 1.29–8.85). Noticeably, post-TKI survival in CML overall approximates that for ALL, whereas therapeutic advancements for AML remain modest.
Conclusion: Registry data show that introduction of molecular therapies coincides with revolutionised therapeutic outcomes in childhood CML entailing dramatically improved survival which is now similar to that in ALL. Given that age disparities in survival remain substantial, offering optimal therapy to entire populations is an urgent priority.

1. Introduction

Childhood chronic myeloid leukaemia (CML) is a rare malignancy accounting for approximately 2% of all leukaemias with increasing incidence by age [1]. CML is characterised by the reciprocal translocation t(9; 22; q34; q11). This genetic abnormality leads to fusion between the ABL1-oncogene in chromosome 9 and the BCR gene in chromosome 22; this fusion causes deregulated ABL1 tyrosine kinase activity. During the last decades, introduction of molecularly targeted therapy which inhibits the BCR/ABL tyrosine kinase activity has revolutionised treatment and prognosis among adults with CML [2]. In particular, imatinib mesylate, a first generation tyrosine kinase inhibitor (TKI), is considered the most successful targeted anti-cancer agent with a high cumulative incidence of complete cytogenetic responses in patients with CML [3].