

SAMPLE ABSTRACT FOR 3Rd ST.JUDE-VIVA FORUM 2009

Successful application of a single PCR-based MRD (PCR-MRD-lite) platform for risk stratification in childhood acute lymphoblastic leukemia (ALL) therapy: Results of the Malaysia-Singapore ALL 2003 study

Authors: KWOK Cecilia S¹, KHAM Shirley Kow-Yin¹, ARIFFIN Hany², CHAN Yiong-Huak¹, YEOH Allen Eng-Juh¹. ¹National University of Singapore, Singapore, ²University of Malaya Medical Centre, Kuala Lumpur, Malaysia.

E-mail: paeyej@nus.edu.sg

Background: Early response to therapy as determined by minimal residual disease (MRD) measurements is the single most important predictor of outcome in childhood acute lymphoblastic leukemia (ALL). PCR-based markers for MRD measurement utilizing Ig/TCR rearrangements are surrogate markers and may undergo clonal evolution which may adversely impact their prognostic value. The aim is to evaluate if this MRD-lite methodology is sufficiently dependable for tailoring therapy, while being cost-effective and applicable to the majority of patients.

Methods: The Malaysia-Singapore ALL 2003, based on modified BFM ALL 2000, utilizes a single PCR-based MRD marker (PCR-MRD-lite). Patients that have MRD $\leq 10^{-4}$ at 5 weeks and 12 weeks are standard risk (SR); patients that have MRD $\geq 10^{-3}$ at 12 weeks, BCR-ABL, MLL-AF4, or prednisolone poor response are high risk (HR); and the remaining patients are intermediate risk (IR). SR patients received deceleration of therapy compared to IR while HR patients received further intensification using the CCG augmented BFM regimen. Identification of MRD markers is done using multiplex BIOMED-2 primers, with hierarchical screening of rearrangements based on frequency and stability of MRD markers.

Results: A total of 198 patients were enrolled in the study from July 2002 to January 2006, with a median age of 4.36 years (range 0.36 to 13.4). There were 5 (2.5%) non-responders, 3 (1.5%) deaths in induction, and 1 (0.5%) lost to follow-up. Of the 189 patients stratified, 33% (n=63) were SR, 42% (n=79) were IR, and 25% (n=47) were HR. MRD stratification was possible for 88% (174/189; insufficient DNA=7; missing time-points=5; no marker=12). At the time of analysis, the median follow-up was 20.8 months (range 1.2-42.7). The overall 3-year event free survival (EFS) was 83%. EFS was 96% for SR, 92% for IR and 50% for HR. Majority of the events (14/22) were in the HR group.

Conclusion: We conclude that a simplified MRD methodology utilizing a single PCR-based marker (PCR-MRD-lite) can be successfully implemented to tailor therapy for childhood ALL more cost-effectively in a larger group of patients without adversely affecting the outcome. This is particularly useful for countries with more limited resources to pursue MRD-based risk stratification.

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