

Title:	Polymerase chain reaction in the diagnosis and monitoring of patients with BCR-ABL gene rearrangement in acute lymphoid leukaemia, March 2004
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Aim

To assess the safety, effectiveness and cost effectiveness of PCR testing for these indications and the circumstances under which public funding should be supported for them.

Conclusions and results

Safety. The PCR assays discussed in this review have no additional safety concerns. The required quantity of blood or marrow is minimal and would usually be collected concurrently with other routine blood or marrow tests.

Effectiveness

Diagnostic accuracy in ALL diagnosis. PCR testing had an estimated sensitivity for the detection of BCR-ABL of 90 per cent compared with 72 per cent for cytogenetic testing alone. PCR was estimated to have a specificity of 97 per cent (95% CI 92, 99). FISH was used as the reference standard and should be regarded as being imperfect.

Diagnostic accuracy in ALL monitoring. PCR was evaluated for its ability to predict subsequent cytogenetic and haematological relapse in the monitoring studies. All six eligible studies were case series. The pooled diagnostic odds ratio (DOR) from these studies was 4.7 (95% CI 2.2, 10.3). A DOR of 4.7 is consistent with, for example, a sensitivity of 80 per cent and specificity of 54 per cent. A median of three months elapsed between classification of PCR positivity and relapse.

Change in management. The use of PCR at presentation provides a sensitive method of detecting BCR-ABL. Patients with BCR-ABL ALL have high risk disease and are treated more aggressively than other ALL patients including the use of matched unrelated donor (MUD) transplants in CR1. In contrast, other patients with ALL would have MUD transplantation reserved until following relapse.

Effect of additional PCR testing on patient outcome. BCR-ABL ALL has a poor prognosis compared with other ALL disease. Therefore, patients are treated more aggressively and the accurate detection of BCR-ABL allows the use of more appropriate therapeutic interventions as a result. Monitoring with PCR was associated with early detection of relapse. However, no specific evidence was found for improved prognosis resulting from early detection of relapse although it is biologically plausible that prognosis would be improved through treatment at levels of lower leukaemic load.

Cost-effectiveness

Diagnosis. The economic analysis evaluating the use of PCR in the diagnosis of ALL found the incremental cost per 4-5 year survival was \$46,616 in adults and \$176,042 in children for cytogenetic and PCR testing compared with cytogenetic testing alone.

Monitoring. There were insufficient data to estimate an incremental cost effectiveness ratio for combined PCR and cytogenetic testing compared with cytogenetic testing alone in monitoring due to lack of data comparing "early" with "late" treatment. However, the estimates of direct testing costs for PCR monitoring were approximately 8 per cent of the cost of monitoring all ALL patients by cytogenetic testing.

Recommendations

MSAC recommended that public funding should be supported for PCR testing in the diagnosis and monitoring of ALL.

Method

A systematic review of the PCR in diagnosis and monitoring of BCR-ABL ALL was conducted. The literature was searched up to June 2003 using Medline, Embase, Current Contents, Cancerlit, Cochrane Library, NHS Centre for Reviews and Dissemination databases and various website sources. Study selection criteria were stipulated and standard checklists were used to appraise study quality.

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