

<b>Title:</b>	<b>Polymerase chain reaction in the diagnosis and monitoring of patients with AML1-ETO and CBF<math>\beta</math>-MYH11 gene rearrangement in acute myeloid leukaemia, August 2003</b>
<b>Agency:</b>	Medical Services Advisory Committee (MSAC) Australian Government Department of Health and Ageing GPO Box 9848 Canberra ACT 2601 Australia <a href="http://www.msac.gov.au">http://www.msac.gov.au</a>
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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.

*Safety.* The PCR assays discussed in this review are unlikely to directly increase risk to patients.

### *Effectiveness*

Diagnostic accuracy in AML diagnosis. In AML1-ETO, 3.0 per cent (95% CI 1.9, 4.6) of all AML cases were PCR positive and cytogenetic test negative. In CBF $\beta$ -MYH11, 1.4 per cent (95% CI 0.9, 2.0) of all AML cases were PCR positive and cytogenetic test negative. PCR was estimated to have a specificity of 99.6 per cent (95% CI 97.8, 100) in AML1-ETO and 99.2 per cent (95% CI 97.3, 99.9) in CBF $\beta$ -MYH11.

Diagnostic accuracy in AML monitoring. PCR was evaluated for its ability to predict cytogenetic and haematological relapse in the monitoring studies. The pooled diagnostic odds ratio (DOR) for AML1-ETO was 8.7 (95% CI 3.4, 22.0) and for CBF $\beta$ -MYH11 the DOR was 35 (95% CI 10, 119). A DOR of 8.7 is consistent with, for example, a sensitivity of 80 per cent and specificity of 69 per cent while a DOR of 35 is consistent with a sensitivity of 95 per cent and specificity of 65 per cent.

Change in management. Appropriate identification of AML1-ETO and CBF $\beta$ -MYH11 determines the therapeutic strategy for patients with these good prognosis abnormalities. Early detection of relapse is more likely to result in different management options compared with late detection due to the lower proportion of patients with comorbid conditions such as sepsis and bleeding and the use of simple interventions such as changing immunosuppressive therapy.

Effect of additional PCR testing on patient outcome. PCR testing detects additional cases of AML1-ETO and CBF $\beta$ -MYH11 not detected by cytogenetic testing. Any additional cases detected by PCR receive a different therapeutic course from patients testing PCR negative. For example, increased dose of ara-C is associated with improved survival and reserving transplantation for salvage therapy has not been associated with poorer overall survival from recent trial data. PCR also predicts haematological relapse early compared with other diagnostic modalities (although with imperfect sensitivity and specificity). There are theoretical advantages to early detection.

### *Cost-effectiveness*

Diagnosis. PCR testing for AML1-ETO and CBF $\beta$ -MYH11 in patients with AML is cost saving based on economic modelling.

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 16 per cent of the cost of monitoring all AML patients by cytogenetic testing.

### **Recommendations**

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

### **Method**

A systematic review of the PCR in diagnosis and monitoring of AML1-ETO and CBF $\beta$ -MYH11 AML was conducted. The literature was searched up to January 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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