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| Title: | Polymerase chain reaction in the diagnosis and monitoring of patients with PML-RARα and PLZF-RARα gene rearrangement in acute promyelocytic leukaemia, March 2003 |
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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 are unlikely to directly increase risk to patients. 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 APL diagnosis. Combined cytogenetic and PCR testing had an estimated sensitivity for the detection of PML-RAR α and PLZF-RAR α of 99 per cent compared with 92 per cent for cytogenetic testing alone, in the studies where cytogenetic testing was successful. PCR was estimated to have a specificity of 100 per cent (95% CI 85, 100).

Diagnostic accuracy in APL monitoring. PCR was evaluated for its ability to predict subsequent cytogenetic and haematological relapse in the monitoring studies. All 16 eligible studies were case series. The pooled diagnostic odds ratio (DOR) from the 13 studies where study DORs could be estimated was 103 (95% CI 57, 186). A DOR of 103 is consistent with, for example, a sensitivity of 92 per cent and specificity of 90 per cent.

Change in management. The use of PCR at presentation provides a sensitive method of confirming the diagnosis of APL as well as differentiating ATRA-sensitive and ATRA-resistant translocations. The early use of salvage therapy for relapse is also supported in the literature.

Effect of additional PCR testing on patient outcome. Identification of PML-RAR α by PCR testing directs therapeutic options to ATRA-based therapy. Therefore, an incremental improvement in diagnostic accuracy at presentation, plus improved differentiation of PML-RAR α from PLZF-RAR α APL, could be expected to produce improved health outcomes given the effectiveness of ATRA in PML-RAR α APL. Monitoring with PCR was associated with early detection of relapse. One study was identified that compared the use of salvage therapy at molecular relapse, detected by PCR, with salvage therapy at haematological relapse, in a historical control series. This study supported improved outcomes with early therapy, that was unlikely to be explained by lead time bias, therefore implying an expectation of improved patient outcomes with the use of PCR in the monitoring of APL.

Cost-effectiveness

Diagnosis. The economic analysis evaluating the use of PCR in the diagnosis of APL found the incremental cost per life year saved was \$329 for cytogenetic and PCR testing compared with cytogenetic testing alone.

Monitoring. The incremental cost per life year saved was \$6,418 for monitoring with cytogenetic plus PCR testing combined, compared with cytogenetic testing alone.

Recommendations

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

Method

A systematic review of the PCR in diagnosis and monitoring of PML-RAR α and PLZF-RAR α APL was conducted. The literature was searched up to November 2002 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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