

Spanish contributions to the management of acute promyelocytic leukemia

A recent Spanish study¹ shows that acute promyelocytic leukemia (APL) may represent about one quarter of all cases of acute myeloid leukemia (AML). This disorder is extremely interesting since a unique t(15;17) chromosome aberration results in the PML/RAR α gene fusion and an exquisite sensitivity to the differentiating agent all-trans retinoic acid (ATRA).² Considerable heterogeneity has been observed at both molecular and clinical level, as shown by previous reports in this journal.³⁻¹²

As clearly summarized by Lo Coco and co-workers,¹³ demonstration of the disease's genetic hallmark can be carried out at chromosomal, protein, DNA or RNA levels, using conventional karyotyping and/or fluorescent *in situ* hybridization (FISH), anti-PML antibodies, Southern blotting and reverse-transcriptase polymerase chain reaction (RT-PCR), respectively. Each of these procedures has its own advantages and pitfalls. In particular, karyotyping may occasionally give false-negative results [i.e. absence of t(15;17) in cases later found to contain cryptic PML/RAR α rearrangement] and like Southern blotting is time-consuming, requiring a few days for execution. RT-PCR allows a rapid and highly sensitive diagnosis, but it is prone to artefacts and technically difficult if not performed in experienced laboratories. In the light of this, the Spanish group has recently designed an external quality assessment program (EQAP) of RT-PCR detection of PML/RAR α , which includes a study of sensitivity of the participating centers. The results, published in this issue¹⁴ point to heterogeneous sensitivity amongst participating laboratories. This may reflect differences in methodology, although variations in sample quality may also account for discrepant findings.

The detection of PML-RAR transcripts by RT-PCR in APL patients who are in hematologic remission influences therapeutic decision making.¹⁵ Although the majority of patients in long-term clinical remission are negative by consecutive RT-PCR assays, negative tests are still observed in patients who ultimately relapse. Conversion from negative to positive PCR has been observed after consolidation and found to be a much stronger predictor of relapse. A second

Spanish study reported in this issue¹⁶ has analyzed the correlation between minimal residual disease (MRD) status and clinical outcome in a cohort of APL patients. This study highlights the prognostic value of RT-PCR monitoring after treatment of APL patients, and suggests that PCR assessments should be carried out at 3-month intervals to provide a more accurate prediction of hematologic relapses but only once treatment has been completed.

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