us /cytoplasm distribution.[3] In fact, differently from PGP, LRP is primarily located in the cytoplasm[4] whereas MRP has been found both at the surface of the cellular plasma membrane, in the cytoplasm and in the Golgi region.[5,6] An additional part of this study was to compare the toxicity of DNX to that of a combination of free DNR plus MDR modifiers, in cell lines showing a non-PGP related MDR. In these MDR cell lines, the addition of MDR modifiers, such as D-verapamil or SDZPSC833, to free DNR only marginally increased the drug's toxicity. Moreover, this increase was smaller than that observed by substituting free DNR with DNX (Table 1). In conclusion, this work shows that the liposomal formulation of DNX doubles DNR toxicity in cell lines with an MDR associated overexpression of MRP or LRP. The increase in DNR toxicity due to the liposome encapsulation is higher than that produced by adding SDZPSC833 or D-verapamil to free anthracycline. These data support the ongoing research into the use of liposomal anthracyclines for the treatment of acute non-lymphocytic leukemia, considering that, even at disease onset, myeloid blast cells often show defects in drugs accumulation associated with co-overexpression of both PGP and LRP.[7-10]

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***Key words***

*LRP, MRP, lung resistance-associated protein, multidrug resistance related protein, acute leukemia, liposome, daunorubicin, multi drug resistance.*

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## Chronic myeloid leukemia in chronic phase with a partial trisomy 9 mosaicism

Sir,

We report a case of CML in chronic phase in a 72-year old woman with a previous history of heart disease and atrial fibrillation. She had a pronounced leukocytosis with a WBC count of $254\times10^9$/L, 1% of blasts and 10% of basophils. Her hematocrit was 33% and platelet count $370\times10^9$/L. Neutrophil alkaline phosphatase (NAF) activity was absent. Bone marow cellularity was increased and the myeloid/erythroid ratio was 1/2. The marrow contained 1% of blast cells.

Cytogenetic study, applying G-band techniques, of the bone marrow revealed the presence of two different cell lines: 60% of the metaphases analyzed were 46,XX,Ph while the remaining 40% had 47 chromosomes and Ph, the excess chromosome being a chromosome 9 with an interstitial deletion in its long arms.

Fluorescence *in situ* hybridization (FISH) was performed on chromosome preparations with two differently labeled bcr/abl translocation DNA probes (Vysis LSI bcr/abl tp). A total of 100-150 cells (metaphase and interphase) were counted. The existence of three signals was proved by the ABL probe, one hybridized to chromosome 9, another to the deleted 9 and the classic ABL/BCR fusion, in its nor-

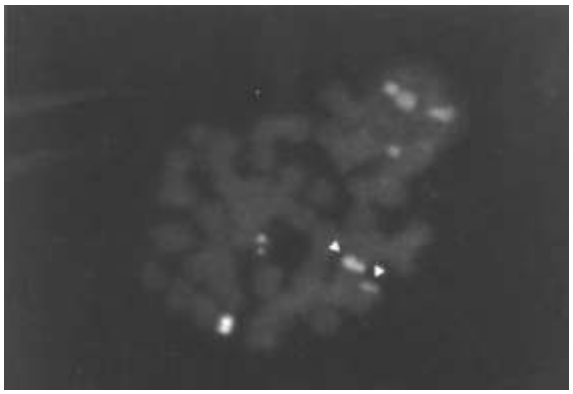

**Figure 1. Metaphase and interphase cells with FISH showing two hybridazation signals for the ABL probe at 9q34 (white arrows), classic fusion ABL/BCR and the BCR probe at 22q11 (Rhodamine/FITC).**

**Figure 2. An interphase cell with FISH showing three hibridization signals for the ABL probe (Rhodamine/DAPI).**

mal position on 22q11 at a slightly higher percentage to the one in the cytogenetic study: 43% metaphase/46% interphase (Figures 1 and 2).

After treating the patient with hydroxyurea and then interferon-α (IFN), the WBC count returned to normal, and blasts disappeared from the peripheral blood. The percentage of basophils remained stable.

The development of clonal cytogenetic abnormalities besides Ph chromosomes in patients in accelerated phase or blastic CML is a sign of imminent disease progression;[1-5] the additional changes are clearly not random and two pathways of cytogenetic evolution may be distinguished: major and minor routes.[3]

Our patient showed a partial 9 trisomy associated with Ph in the chronic phase at the time of diagnosis. The presence of this abnormality led us to believe that the patient would develop an acceleration of her chronic phase. However there was a hematologic remission after treatment.

According to O'Brien *et al*.[6] clonal evolution is infrequent in the chronic phase and its significance depends on the specific chromosome involved, the number of metaphases affected and the timing in the chronic phase. We are unable to assert what the role of partial trisomy 9 in a Ph positive patient really is in the evaluation of CML on the basis of this unique case (we have found no other descriptions of this combination of abnormalities).

FISH allowed us to prove that the trisomy was present at a slightly higher percentage, and corroborated that the partial trisomy 9 was interstitial as a signal for the abl probe at 9q34. The ABL/BCR probe was also used to investigate whether the traslocation was a classical one, since complex molecular rearrangements can appear in 5-10% of patients with CML.[3,7]

The use of dual color FISH in the diagnosis of CML is extremely valuable not only in identifying cases of Ph-negative CML (this information gives well defined results), so enabling us to follow disease progression. It is also essential to evaluate minimal residual disease and quantify the proportion of the transformed cell population.

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***Key words***

*CML, trisomy 9 mosaicism, FISH*

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