PATTERN OF CNS RELAPSE IN ACUTE LYMPHOBlastic LEUKEMIA

Background: We have performed massive sequencing experiments of ABL1 Kinase domain associated with CNS relapse probability. In two of the CNS and BM relapsed patients we have observed variants of uncertain significance (VUS) in kinase domain of the BCR-ABL from cDNA of cerebrospinal fluid (CSF), in order to adapt the TKI used in relapse according to the clonal evolution from bone marrow (BM) to CSF cells.

Methods: We have reviewed data of CNS relapse of patients included in two consecutive clinical trials of the PETHEMA group using imatinib and chemotherapy. As secondary objective we proposed the introduction of a new method for the study of variants of uncertain significance (VUS) in kinase domain of the BCR-ABL from cDNA of cerebrospinal fluid (CSF) blasts, in order to adapt the TKI used in relapse according to the clonal evolution from bone marrow (BM) to CSF cells.

Results: In our series we did not find any clinical variable predicting CNS relapse. We have found the pathogenic variant p.L387M in CSF blasts of two patients with combined CNS and BM recurrence, this variant not being found in BM samples at diagnosis or at relapse. These mutations were sensitive to other TKIs with better penetration to CNS. Based on these results, a mutational study of the kinase domain of the BCR-ABL in blast cells obtained from CSF should also be integrated in the mutation study of these patients in order to select the TKI according to the clonal evolution from BM to CSF cells.

E866 PROGNOSTIC IMPACT OF COPY NUMBER ALTERATIONS IN A SERIES OF PEDIATRIC PATIENTS WITH DE NOVO B-CELL PRECURSOR ACUTE LYMPHOBlastic LEUKEMIA IN A SINGLE CENTER

Background: Gene copy number alterations (CNAs) have been recently proposed as predictors of minimal residual disease (MRD) in pediatric B-ALL. However, their use in clinical practice is controversial, as their prognostic impact could depend on the applied therapeutical protocol and the interaction with other clinical and biological variables.

Aims: To analyze the prognostic impact of CNAs in a series of pediatric patients with B-cell precursor ALL (pre-B ALL) treated in a single center.

Methods: Pediatric patients (0-18 years) pre-B ALL, diagnosed between 1999 and 2015 and homogeneously treated according to consecutive protocols of the Spanish Hematology and Oncology Pediatric Society (SEHOP) Cooperative Group (SHOP-99, SHOP-2005, SEHOP-PETHEMA 2013).

Results: We included 55 patients with a median age of 4.7 years (range 1.1-14.9), 56% males. Only one patient had central nervous system infiltration. Median WBC count was 8.4x10^9/L (range 1.1-296.9). All cytogenetic subtypes were represented. We observed the presence of CNAs in 29 patients (53%), including 17 (31%) cases with one CNA, 8 (15%) patients with 2 CNAs and 4 (7%) patients with ≥3 CNAs.

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