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THE LONG-TERM DURABILITY OF MOLECULAR RESPONSES IN PATIENTS WITH FIP1L1-PDGFRα CHRONIC HEPATOMONOPHILIC LEUKEMIA TREATED WITH IMATINIB: THE ITALIAN HES0203 EXPERIENCE AFTER A 4-YEAR FOLLOW-UP


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Imatinib mesylate is the first line treatment for hyperesinophilic syndrome with FIP1L1-PDGFRα (F/P) fusion gene. Few clinical and molecular data on the outcome of patients with FIP1L1-PDGFRα positive CEL treated with imatinib are available to evaluate the long term follow up of patients and to evaluate the clinical correlation with different transcripts of fusion gene. A prospective phase 2 multicenter study of the use of imatinib 400 mg/day in patients with hyperesinophilic syndrome, irrespectably of F/P status was established in 2001. 72 patients were treated with IM 100 to 400 mg daily; the 33 F/P positive patients (F/P+) were regularly monitored with nested RT-PCR. The observation period of F/P+ patients ranges between 23 and 85 months (median 48 months). There were 32 males and one female patient. Organ involvement was recorded in 43% of F/P+. After imatinib therapy all patients achieved a complete hematologic response (CHR) in less than one month, and PCR negativity in a median time of 3 months. They became negative for organ localizations and free of symptoms. All patients who continue imatinib therapy remain in CHR and RT-PCR negative, with a dose of 100 to 400 mg daily. From September 2007 all patients except one (late responder) were treated with 100 mg daily. In six patients IM treatment was discontinued for variable period for different reasons, and in 5 cases the fusion transcript became rapidly detectable. CHR was maintained, other than in one case. The transcript was again undetectable upon treatment resumption, other than in one case. All samples were valuable for molecular analysis. Fusion gene sequencing demonstrate an extreme variability of FIP1L1-PDGFRα junction sequences, but with no correlation with kinetic of molecular response or with the presence at diagnosis of peculiar organ involvement. More complexity of transcript is not ed in patients with longer history of disease prior to imatinib therapy. With this large series of patients we can confirm the extremely sensitivity of F/P+ CEL to imatinib therapy, without any significant toxicity after protracted therapy and without acquisition of resistance. The complexity and variability in FIP1L1-PDGFRα transcripts seems to no correlate with phenotype of disease, even though different kinetic of response have been observed. Prolonged clinical and molecular follow-up of these patients is essential to understand the CEL disease.

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BUSULFAN-MELPHALAN AND AUTOLOGOUS STEM CELL TRANSPLANTATION IN AML PATIENTS IN FIRST CR: A “GRUPPO ITALIANO TRAPIANTO DI MIDOLLO OSSEO (GITMO)” RETROSPECTIVE STUDY


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Acute myelogenous leukemia (AML) patients (=129; median age =50 years; range 16-72) in first complete remission (CR) received busulphan and melphalan (Bu/Mel) as conditioning regimen prior autologous stem cell transplantation (ASCT). Eighty two patients (63.6%) received peripheral blood stem cells (PBSCs) and 47 patients (36.4%) received bone marrow (BM) cells. Cytogenetic categories distribution was conventionally defined as favorable (15.5%); intermediate (60.1%) and unfavorable (24.3%). With a median follow-up of 31 months, the 8-years projected overall survival (OS) and disease-free survival (DFS) was 62% and 56% for the whole population, respectively. The relapse rate was 46% and the non-relapse mortality was 4.65%. Although PBSC transplantation led to a faster hematological recovery than BM transplantation, in univariate analysis the stem cell source, cytogenetics and different busulphan formulations did not significantly affect OS and DFS whereas age and the number of post-remission chemotherapy cycles did have significant impact on the clinical outcome. Multivariate analysis identified age < 55 years as the only important independent predictor for OS and DFS. Our data suggest that Bu/Mel is an effective conditioning regimen even for high risk AML patients in first CR undergoing ASCT being associated with a low toxicity profile (mainly mucositis) and mortality.

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A PHASE II MONOCENTRIC STUDY OF MODIFIED BEAM REGIMEN FOR HODGKIN’S DISEASE AND NON-HODGKIN’S LYMPHOMAS

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The intensive therapy followed by an autologous transplant of hematopoietic stem cells (HSCs) is and has been widely used for the treatment of Hodgkin’s and non-Hodgkin’s lymphoma, with the intent of increasing the number of patients cured in first line treatment with high risk disease including those non completely responsive to first line treatment or relapsed cases. For over 25 years the therapy most widely used as conditioning regimen for autologous HSCs transplant of lymphomas is the BEAM protocol, which foresees the administration of Nitrumon 300 mg/sm day -6, Cytosine Arabinoside (Ara-C) 200 or 400 mg/sm and Etoposide 200 mg/sm once a day from day -5 to day -2 and Melphalan 140 mg/sm day -1. Ara-C, when used in the scheme of therapy for the treatment of lymphomas is administered in high doses (1-2 gr/sm) because its known to be more effective. With the intention to increase the efficiency of the BEAM protocol, we have modified the treatment schedule accordingly: Nitrumon 300 mg/sm day -5, Ara-C 2 gr/sm and Etoposide 200 mg/sm once a day for 3 days from -4 to -2 and Melphalan 140 mg/sm day -1. The aim in this first phase of the study was to evaluate the toxicity of the treatment and the resumption of the myeloipoiesis. From April 2007 until January 2009 we treated 20 patients.