O.6 Long-term survival in patients receiving rhEPO following allogeneic hematopoietic cell transplantation

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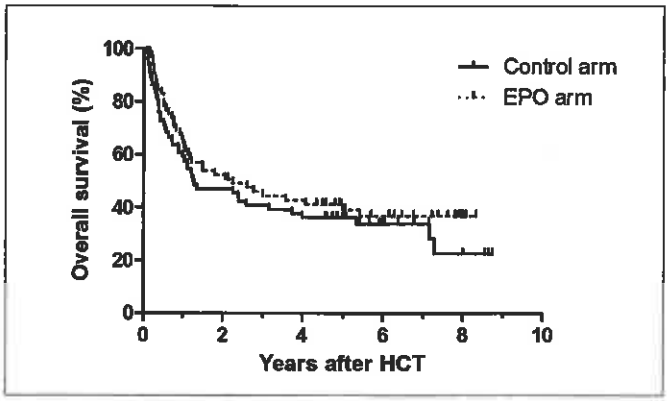
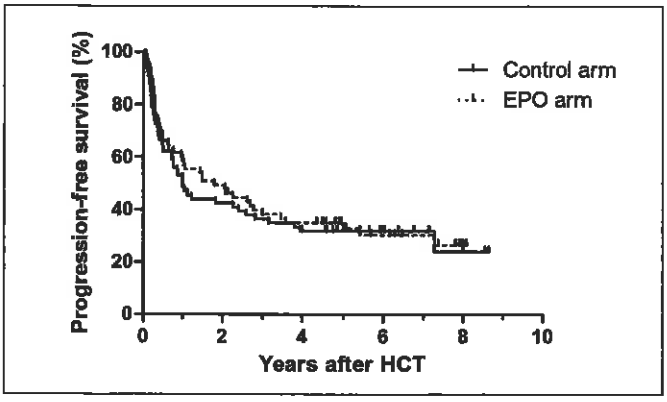
We recently reported the efficacy of erythropoietin therapy following allogeneic hematopoietic cell transplantation (allo-HCT) on erythroid reconstitution and transfusion requirements. As some meta-analyzes suggest increased mortality in patients with cancer receiving erythropoiesis-stimulating agents (ESA) particularly when no concomitant chemotherapy is administered, we assessed long-term follow-up of patients included in the study.

In this trial, 131 patients given myeloablative or non-myeloablative allo-HCT were randomized 1:1 between two arms: the control arm (no erythropoietic therapy) vs the EPO arm (erythropoietin β 500 U/kg/week). Patients were also stratified in 3 cohorts : 42 patients underwent myeloablative HCT (cohort A), while patients in the cohorts B (n=39) and C (n=50) were given non-myeloablative conditioning. RhEPO was administered once a week, from day 28 in cohorts A and B, whereas patients in cohort C received rhEPO from day 0. Treatment duration was initially planned for 16 weeks but there were rules for decreasing or withholding rhEPO according to the Hb level.

The total number of injections of rhEPO until day 126 was 12.6 ± 4.6. After day 126, 19 patients received maintenance therapy with the lowest possible dose of rhEPO. Median times to reach Hb ≥ 13 g/dL, ≥ 12 g/dL or +2 g/dL were shorter in the EPO arm and this resulted in a reduction of transfusion requirements in the EPO arm. After a median follow-up of 655 days, we did not observe any difference in rates of overall survival (OS). Indeed, 1-year and 5-year OS were 59% and 36% in the control arm and 65% and 39% in the EPO arm (p=0.33) (figure 1). Progression-free survival (PFS) was also similar in the two arms: 1-year and 5-year PFS were 48% and 31% in the control arm and 58% and 32% in the EPO arm (p=0.64) (figure 2).



O.6 *Figure 1.* Overall survival after HCT



O.6 *Figure 2.* Progression-free survival after HCT

In conclusion, rhEPO following allo-HCT did not have an impact on survival in long-term analyses.

O.7 NOTCH1 c.7544-7545 delCt mutation identifies a subgroup of lymphocytic leukemia patients with poor outcome

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NOTCH1 has been found recurrently mutated in a subset of patients with chronic lymphocytic leukemia (CLL). Recent studies showed that activating mutations of NOTCH1 proto-oncogene occur in about 10% CLL at diagnosis and are associated with an unfavorable clinical outcome (Rossi et al, 2012).

We have investigated 105 samples (collected between 2008-2013) of CLL patients for the NOTCH1 mutation: c.7544-7545 delCt. The NOTCH1 mutation was investigated by amplification refractory mutation system (ARMS) PCR of the CLL patients at diagnosis, with a median age of 65 years (range 40-87), 60 males and 45 females. Additionally other prognostic markers in CLL have been investigated. FISH analysis was performed for the detection of trisomy 12, deletion 11q, deletion 13q and deletion 17p. The IGHV gene mutational status was performed by DNA sequencing.

We found NOTCH1 c.7544-7545 delCt mutations in 16.2 % of the cases. The results of the NOTCH1 mutation analysis were compared with the results of the other prognostic factors as trisomy 12, deletion 11q, deletion 13q, deletion 17p and IGHV gene mutation status. All patients harboring a NOTCH1 mutation and consequently had a poor prognosis did not show a deletion 13q as the sole aberration which is connected with a good prognosis. Trisomy 12, deletion 11q, deletion 17p have been found in NOTCH1 mutated as well as in NOTCH1 wild type cases. Half of all cases show an unmutated IGHV gene and/or a c.7544-7545 delCt mutation which predicts a poor outcome.

NOTCH1 seems to be an independent predictive marker for poor outcome in CLL patients. Because of the importance as prognostic marker in CLL the NOTCH1 c.7544-7545 delCt analyses is included in our spectrum of tests for CLL patients. In the future the follow-up of the patients will give us more information of the clinical impact of the NOTCH1 mutation.

O.8 JAK2 V617F-Negative AND MPL W515K/L-Negative Essential Thrombocythemia: a High Resolution SNP Array Study

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Background

JAK2 V617 and *MPL* W515K/L are the most common mutations in essential thrombocythemia (ET), occurring in approximately 60 % of cases. The molecular cause of the remaining ET cases is still largely unknown.

Aims

We sought to investigate *JAK2* V617F-negative and *MPL* W515K/L-negative ET for regions of copy number variations (CNV) and loss of heterozygosity (LOH).

Methods

We studied blood or bone marrow samples from a series of 64 *JAK2* V617F-negative and *MPL* W515K/L-negative ET cases. They