

# Diagnosis of Chronic Myeloid Leukemia Early in Pregnancy

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## ABSTRACT

*Imatinib therapy has revolutionized the clinical course of Chronic Myeloid Leukemia. The unexpected prolonged survival raised several issues on the quality of life and on the possibility to parent childs.*

**Keywords:** Chronic Myeloid Leukemia, Pregnancy, Therapy, BCR-ABL

## 1. Introduction

The introduction of the tyrosine kinase inhibitor Imatinib Mesylate (IM) for the treatment of Chronic Myeloid Leukemia (CML) in chronic phase (CP) resulted in high rates of hematologic, cytogenetic and molecular responses [1]. Furthermore, clinical long term follow up has shown an estimated 8-year overall survival of 85% for patients receiving IM on an intention to treat basis [2]. These spectacular results led CML patients not only to a prolonged survival but also to drive relatively normal lives. In this view, several issues on the quality of life and, among them, on fertility and pregnancy have been raised. Here we report the case of a female patient who was incidentally diagnosed with CML while early in pregnancy and who wanted to get gestation to term.

## 2. Case Report

A 41 year-old female was referred to our Institution because of severe leukocytosis. She was at the 10<sup>th</sup> week of gestation and at physical examination presented only a mild splenomegaly (1 cm below costal margin) without any lymph nodes enlargement. Laboratory exams revealed a white blood cell (WBC) count of  $146.3 \times 10^9/L$ , a platelet cell count of  $820.0 \times 10^9/L$ , a hemoglobin concentration of 10.1 g/dL and lactic acid dehydrogenase of 1440 UI/L. The differential WBC showed the presence of immature myeloid circulating cells (metamyelocytes 11%, myelocytes 13%, promyelocytes 3% and blasts 2%), while bone marrow cytogenetic showed the presence of

the Philadelphia (Ph)-positive chromosome in all the examined metaphases with no further abnormalities. The patient was then diagnosed as having CP-CML, intermediate Sokal risk with a e13a2 *BCR-ABL*-transcript and a *BCR-ABL/ABL* % ratio of 107.62 on the International Standardized Scale (IS). Since the patient wanted to carry pregnancy to term, she started cyto-reduction, with five weekly leukapheresis, and thrombosis prophylaxis with low dose low molecular weight heparin (Clivarin 1750 U) every 12 hours. From the 23<sup>rd</sup> week of gestation she begun  $\alpha$ -interferon-treatment ( $\alpha$ -IFN; 5MUI daily), obtaining soon a complete hematological remission (CHR).  $\alpha$ -IFN-therapy was interrupted at the 37<sup>th</sup> week of gestation since a cesarean delivery was scheduled at the 38<sup>th</sup> week, when the patient gave birth to a healthy baby. After fifteen days from delivery and while still in CHR, she started conventional IM-therapy (400 mg daily). *BCR-ABL/ABL* transcript levels were 46.52<sup>IS</sup> at that time and decreased to 10.26<sup>IS</sup> at the third month of therapy. She is presently alive and well on standard IM treatment.

## 3. Conclusions

The radical improvements in the long-term survival of CML patients now pose novel medical challenges. Treating physicians will have to manage IM long-term side effects [3] as well as simultaneous chronic illnesses in an aging CML population. Moreover, the higher rates of molecular remission coupled with a relatively normal quality of life raised in some CML patients the issue on the ability to parent children. On this address a recent cumulative experience has been published on CML pa-

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tients conceiving while taking IM [4]. Nevertheless the CML management during pregnancy remains still a clinical challenge and no systematic clinical studies are described. Here we report a pregnant woman whose CP-CML disease was incidentally diagnosed while early in gestation and who wanted to carry her pregnancy to term. A similar clinical case has been reported by Cole S. and colleagues [5] whereas Björkholm M. *et al.* described a CML patient presenting late in pregnancy [6]. However our patient had an intermediate Sokal risk, a high *BCR-ABL/ABL* transcript at diagnosis (both representative of aggressive leukemic burden) and an increasing WBC-count: these two relevant clinical events prompted us to consider a proper therapeutical intervention.

Since the use of both hydroxyurea and IM is not recommended during gestation, we started cytoreduction with leukapheresis and introduced  $\alpha$ -IFN therapy, which reduced *BCR-ABL/ABL* transcript levels from  $107.62^{IS}$  to  $46.52^{IS}$ . Therefore, on the basis of our clinical experience, we believe that  $\alpha$ -IFN-treatment might be a useful tool in the management of early pregnancy during CML. However, when a CML female patient wants to conceive, the best choice could be to start IM-therapy, to achieve a major molecular response, or better a complete molecular response, and then to stop treatment attempting to conceive.

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