

# A CML Patient with Unintentional Bosutinib Exposure During the First Trimester of Pregnancy

## Gebeliğin İlk Trimesteri Boyunca Farkında Olmadan Bosutinibe Maruz Kalan KML Hastası

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### To the Editor,

Chronic myeloid leukemia (CML) is a BCR-ABL1-driven myeloproliferative neoplasm that predominantly affects adults; however, an increasing number of cases are diagnosed in women of reproductive age [1]. The management of CML during pregnancy remains challenging due to the potential teratogenic effects of tyrosine kinase inhibitors (TKIs), particularly during the first trimester. Current recommendations advise discontinuation of TKIs upon confirmation of pregnancy, with close monitoring and consideration of interferon- $\alpha$  when treatment is required [1,2]. These recommendations are consistent with the 2020 European LeukemiaNet guidelines for the management of CML [3]. Data on newer TKIs, including bosutinib, are extremely limited, and their use during pregnancy is generally discouraged.

We report a 37-year-old woman with CML who conceived while receiving bosutinib and subsequently delivered a healthy infant. The patient was initially diagnosed after incidental leukocytosis and thrombocytosis, with a BCR-ABL1 transcript level of 11.3% and a low EUTOS Long-Term Survival score (Table 1). First-line imatinib therapy was complicated by grade 3 neutropenia

and cutaneous toxicity, necessitating dose reduction and intermittent treatment interruptions due to intolerance. Due to loss of molecular response at 6 months, treatment was switched to bosutinib (500 mg/day). Tyrosine kinase domain mutation analysis was not performed prior to initiating bosutinib, as the suboptimal molecular response was attributed primarily to treatment intolerance and irregular imatinib exposure rather than suspected primary resistance. Despite counseling on contraception, the patient unknowingly continued using bosutinib during early pregnancy.

Pregnancy was recognized approximately 3 months after bosutinib initiation and the drug was discontinued at 12 weeks of gestation. Non-invasive prenatal testing (NIPT) revealed a rare autosomal abnormality consistent with monosomy 7. However, detailed fetal evaluation, including ultrasound, amniocentesis, karyotyping, and chromosomal microarray analysis, showed normal results. During pregnancy, the patient was closely monitored with monthly follow-up visits. No loss of hematological response or clinical deterioration was observed and BCR-ABL1 transcript levels remained stable throughout pregnancy. Initiation of imatinib therapy after the third trimester

**Table 1. Timeline of BCR-ABL1 transcript levels in relation to treatment and pregnancy course.**

Date	Gestational status	BCR-ABL1 IS (%)	Timeline
October 2023	Not pregnant	11.3	At diagnosis
January 2024	Not pregnant	7.4	At 3 months of imatinib (dose reduced due to toxicity)
April 2024	Periconception period	22.28	At 6 months of imatinib, loss of molecular response → switched to bosutinib
July 2024	~12 weeks	5.5	Pregnancy recognized, bosutinib discontinued
October 2024	24 weeks	4.5	Treatment-free monitoring during pregnancy, molecular levels remained stable
January 2025	38 weeks of gestation (term)	4.1	Term delivery by repeat cesarean; healthy male infant
April 2025	3 months postpartum	11.89	Molecular relapse postpartum; bosutinib restarted
July 2025	6 months postpartum	0.16	Bosutinib 500 mg once daily
October 2025	9 months postpartum	0.01	Deep molecular response achieved

IS: International Scale.

was discussed with the patient; however, she declined imatinib treatment. Interferon- $\alpha$  therapy was also not administered due to limited availability throughout pregnancy, and the patient was therefore managed with close monitoring.

At 38 weeks, a healthy male infant was delivered via cesarean section with no congenital anomalies. Postnatal follow-up up to 11 months demonstrated normal growth and neurodevelopment. Further investigations, including placental and maternal genetic analyses, did not identify the source of the monosomy 7 detected by NIPT.

This case adds to the very limited literature on bosutinib exposure during pregnancy. Available data suggest that, unlike imatinib and nilotinib, bosutinib may have a higher potential for placental transfer, although human evidence remains scarce [4,5,6]. In previously reported cases, bosutinib exposure early in pregnancy was not associated with congenital malformations, particularly when discontinued after pregnancy recognition [7].

An additional notable finding in this case was the discordant NIPT result. Maternal malignancies, including hematological cancers, are known to contribute to false-positive NIPT findings due to circulating tumor-derived cell-free DNA [8]. Despite extensive evaluation, the origin of the monosomy 7 signal could not be determined, highlighting the diagnostic challenges in such cases.

In conclusion, this report describes a successful pregnancy outcome following first-trimester exposure to bosutinib in a patient with CML, without apparent teratogenic effects. It also underscores the potential for misleading NIPT results in the context of maternal malignancy. Further accumulation of real-world data is essential to better inform the management of CML during pregnancy and to clarify the safety profile of newer TKIs. However, TKI therapy during pregnancy should be considered with caution and is generally avoided, particularly during the first trimester. Evidence regarding bosutinib exposure during pregnancy remains scarce and its use is discouraged, particularly given its relatively high placental transfer and limited safety data.

**Keywords:** Chronic myeloid leukemia, Pregnancy, Bosutinib, Tyrosine kinase inhibitors, Non-invasive prenatal testing

**Anahtar Sözcükler:** Kronik miyeloid lösemi, Gebelik, Bosutinib, Tirozin kinaz inhibitörleri, Non-invazif prenatal test

## Ethics

**Informed Consent:** Written informed consent was obtained from the patient for the anonymous publication of the case details for scientific purposes.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: G.N.K.Ö., Ö.M., K.M.; Concept: G.N.K.Ö., E.T.D.; Design: G.N.K.Ö., E.T.D.; Data Collection or Processing: G.N.K.Ö., Ö.M., K.M.; Analysis or Interpretation: G.N.K.Ö., E.T.D., Ö.M., K.M.; Literature Search: G.N.K.Ö., Ö.M., K.M.; Writing: G.N.K.Ö., E.T.D., Ö.M., K.M.

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