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LETTER TO THE EDITOR

Imatinib in breast milk

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Dear Editor,

To our knowledge, not much is known about imatinib (IM) treatment and pregnancy, child birth, and breast feeding. Pye and colleagues recently investigated the treatment, pregnancy, and fetal outcomes of 180 women exposed to imatinib during pregnancy. There were a total of 12 infants in whom abnormalities were identified. It appeared that, although most pregnancies exposed to imatinib are likely to have a successful outcome, an element of risk remains for exposure to result in serious fetal malformations [1]. We should like to share the results of measuring imatinib levels in the breast milk of a woman treated with imatinib, even though our findings are related to neonatal rather than fetal drug exposure.

A 34-year-old woman was diagnosed with chronic myeloid leukemia (CML) in chronic phase in 2001 and started on interferon (IFN) alpha of three million units per day at a regional hospital. IFN was well tolerated and the patient achieved complete hematological remission but no major cytogenetic response. In February 2004, the patient was referred to our institution because Bcr-Abl was detectable in 75% of peripheral blood cells by fluorescence in situ hybridization analysis. The patient was started on imatinib of 400 mg/day. Between February and May 2004, molecular monitoring yielded a 1-log decrease in Bcr-Abl messenger RNA (mRNA). In June 2004, the patient reported that she was pregnant. Imatinib was discontinued. As the molecular monitoring in July showed a further 1-log decrease in Bcr-Abl mRNA, no further CML treatment was given during pregnancy. Bcr-Abl transcripts increased up to the May 2004 level only towards the end of pregnancy. A healthy child was born at term. No malformations were detectable. After delivery, imatinib was immediately restarted at 400mg/day. The infant received bottle feeding from the start. However, we asked the mother to defer ablactation until 171 h of imatinib treatment in order to obtain measurements of IM and its active metabolite *N*-desmethyl-imatinib (*N*-DesM-IM, CGP74588) in plasma and breast milk. Drug levels were measured repeatedly (see Table 1). We found that the level of imatinib in breast milk was about half the plasma level. The active metabolite *N*-DesM-IM accumulated about threefold in breast milk as compared to plasma levels. A pseudo-steady-state level was reached in the breast milk after about 2 days of imatinib

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Table 1 Drug level measure

Time after therapy start (h)	IM plasma concentration (ng/ml)	*N*-DesM-IM plasma concentration (ng/ml)	Plasma ratio *N*-DesM-IM/IM (%)	IM breast milk concentration (ng/ml)	*N*-DesM-IM breast milk concentration (ng/ml)	Breast milk ratio *N*-DesM-IM/IM (%)
0	0	0	0	0	0	0
3	1,301	177	14	751	409	54
27	2,482	334	13	1,057	791	75
51	2,010	284	14	1,153	1,024	89
171	2,003	301	15	797	1,052	132

treatment. According to our results, breastfeeding cannot be recommended during treatment with imatinib.

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References

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