Letter to the editor

Imatinib in Breast Milk

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Dear Editor,

Pye and colleagues recently investigated the treatment, pregnancy, and fetal outcomes of 180 woman 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, there remains a risk that exposure may result in serious fetal malformations[1]. To our knowledge, not much is known about a related topic, namely imatinib therapy during breast feeding. We would like to share the results we obtained in measuring imatinib levels in the breast milk of a woman treated with imatinib.

A 34-year-old woman was diagnosed with chronic myeloid leukemia (CML) in chronic phase in 2001 and was started on interferon alpha (IFN) 3 million units per day at another hospital. She tolerated IFN well, achieved a complete hematological remission but did not show a

major cytogenetic response. In February, 2004, the patient was referred to us because FISH analysis of peripheral blood cells had shown 75% of cells positive for BCR-ABL. We started the patient on imatinib 400 mg/d. Between February and May, 2004, molecular monitoring yielded a 1-log decrease in bcr-abl mRNA. In June, 2004, the patient was pregnant. Imatinib was discontinued. As the molecular monitoring in July showed a further 1-log-decrease in bcr-abl mRNA, and transcript levels only climbed back to the May 2004 level towards the end of pregnancy, no further CML treatment was given during pregnancy. A healthy child was born at term. No malformations were detectable. After delivery, imatinib was immediately restarted at 400mg/d. The infant received bottle-feeding from the beginning, but we asked the mother to defer ablactation until 171 hours of imatinib treatment in order to obtain measurements of imatinib (IM) and its active metabolite N-desmethyl-imatinib (CGP74588, N-DesM-IM) 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 3-fold in breast milk as compared to plasma levels. Pseudo-steady-state level in breast milk was reached after about two days of imatinib treatment. According to our results, breastfeeding cannot be recommended during treatment with imatinib.

Table 1

Time after therapy start in h	IM plasma concentration in ng/ml	N-DesM-IM plasma concentration in ng/ml	Plasma ratio N-DesM-IM/IM in %	IM breast milk concentration in ng/ml	N-DesM-IM breast milk concentration in ng/ml	Breast milk ratio N-DesM-IM/IM in %
0	0	0	0	0	0	0
3	1301	177	14	751	409	54
27	2482	334	13	1057	791	75
51	2010	284	14	1153	1024	89
171	2003	301	15	797	1052	132

1. Pye SM, Cortes J, Ault P, et al. The effects of imatinib on pregnancy outcome. Blood. 2008;111:5505-5508.