

Young woman with good response to imatinib wishing to get pregnant

Andreas Hochhaus

EUTOS for CML



European Treatment and Outcome Study

- **28 year-old woman, Ph+ CML, chronic phase,
in January 2004**
Low Sokal and Euro scores
- **Imatinib (400 mg daily): confirmed CCyR (at 12 months)
and 'CMR' (Nested PCR negative) after 18 and 24 months
on imatinib, she is continuing imatinib, very well tolerated**
- **April 2006 (after 25 months on treatment)**
she informs you
OF A STRONG DESIRE TO BECOME PREGNANT

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How would you advise this patient?

1. **No option for pregnancy. Imatinib is teratogenic!**
2. **Imatinib wash-out for 3 months then attempt a pregnancy. No treatment. Imatinib will be restarted after delivery.**
3. **Imatinib wash-out for 3 months then attempt a pregnancy. LOW DOSE INTERFERON AS MAINTENANCE. Imatinib will be restarted after delivery.**
4. **Stop imatinib and attempt pregnancy. No treatment. Imatinib will be restarted after delivery.**
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Summary of available data (n=180)

Timing of exposure to imatinib by trimester known in 146 cases (81%)

71% of these were exposed in the 1st trimester (includes 4 cases exposed in 1st and 2nd trimesters)

**26% exposed throughout their pregnancy
3% exposed after 1st trimester**

Pye et al. Blood. 2008; 111(12): 5505-8

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Imatinib pregnancies

Table 1. Imatinib pregnancies

Pregnancy outcome	Timing of exposure in pregnancy by trimester, no. of patients					Subtotal
	Before LMP	First trimester	After first trimester	Throughout pregnancy	Unknown	
Spontaneous abortion	0	8	0	7	3	18
Elective termination						
Fetal defects	0	1	0	1*	1	3
Normal or unknown	0	20	0	5	7	32
Stillbirth with fetal defects	0	1	0	0	0	1
Live birth with congenital anomaly	0	6	0	0	2	8
Live birth without congenital anomaly	0	40†	1	18	4	63
Outcome unknown	1	27	3	7	17	55
Total	1	103	4	38	34	180

Pye et al. *Blood*. 2008; 111(12):5505-8

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Outcome Known for 125/180 (63%)

Pregnancy outcome	Total number	(%) of those with known outcome n=125	(%) of total n=180
Normal Live Infant	63	50	35
Elective Termination*	35	28	19.5
Fetal Abnormality	12	9.6	6.7
Spontaneous Abortion	18	14.4	10

Pye et al. Blood. 2008; 111(12):5505-8

* Includes 3 terminated following identification of fetal abnormalities

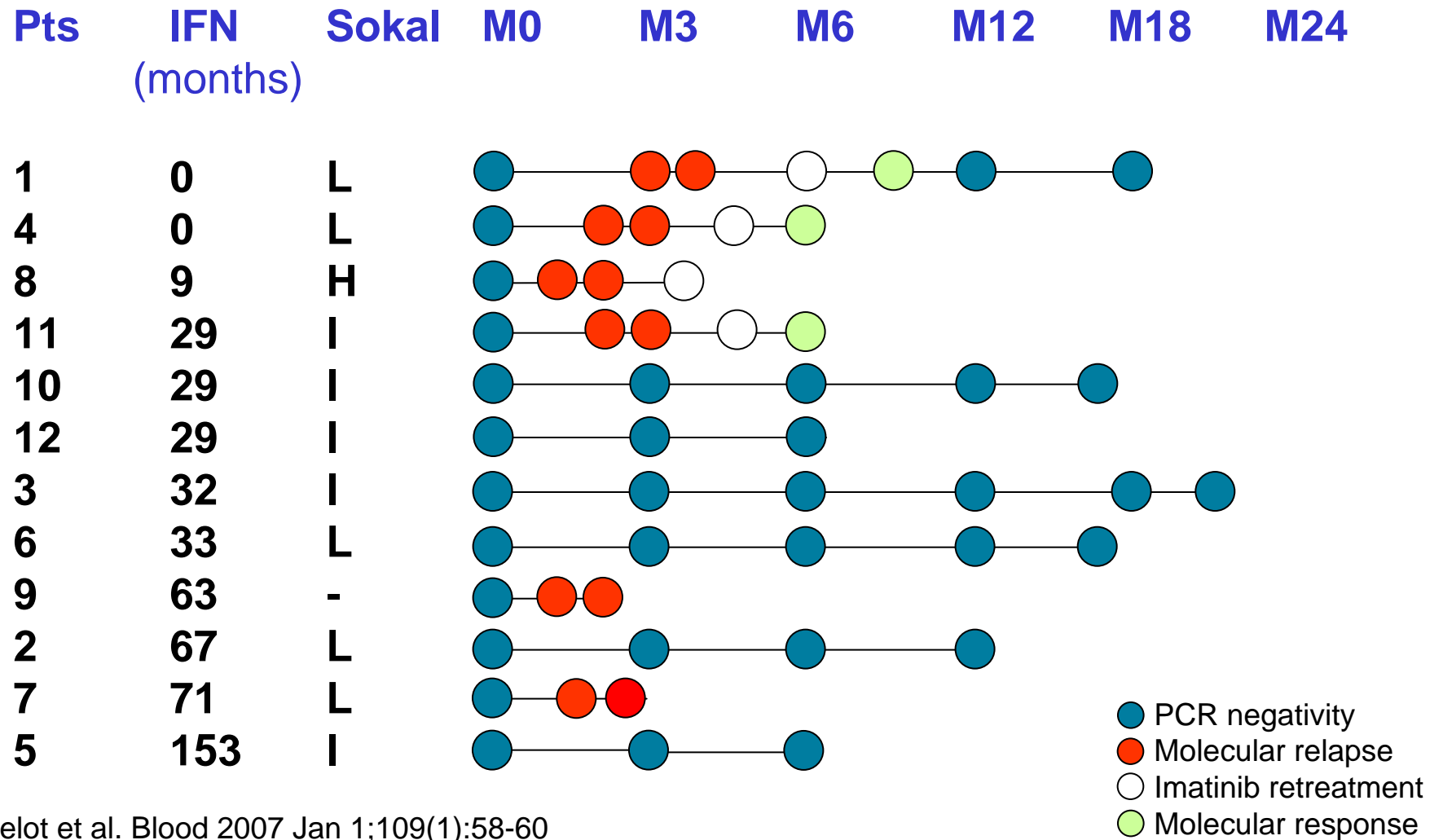
Summary of congenital defects identified following maternal exposure to imatinib (n=12)

Table 2. Summary of congenital defects identified following maternal exposure to imatinib (n = 12)

Fetus no.	Trimester exposure	Pregnancy outcome	Maternal age, y	Imatinib dose (OD), mg	Other medication	Fetal abnormality
1	First	Elective termination	29	300	None	Abnormal ultrasound, elevated AFP
2	All	Elective termination	35	NK	Warfarin, paracetamol, levofloxacin, lorazepam, heparin, prochlorperazine	Warfarin embryopathy: depressed nasal bridge, choanal stenosis, Dandy Walker cyst, ventricular septal defect, coarctation of the aorta, gastroschisis
3	Unknown	Elective termination	37	400	Omeprazole	Cleft palate, polydactyly
4	First	Stillbirth at 34 wk	25	400	Hydroxyurea after first trimester	Meningocele
5	First	Live birth	35	400	Hydroxyurea	Premature closure of skull sutures
6	First	Live birth	Unknown	NK	None	Scoliosis, small exomphalos
7	First	Live birth, premature at week 30: baby died after 45 min	25	400	NK	Communicating hydrocephalus, cerebellar hypoplasia, atrial septal defect, overriding aorta, ascites, pericardial effusion
8	First	Live birth	27	300	Anagrelide and hydroxyurea (timing unknown)	Hypospadias
9	First	Live birth	29	300	None	Hypospadias
10	First	Live birth	35	400	Hydroxyurea after first trimester	Pyloric stenosis
11	First	Live birth	Unknown	400	None	Hypoplastic lungs, exomphalos, left duplex kidney, right absent kidney, hemivertebrae, and right shoulder anomaly
12	Unknown	Live birth (premature)	Unknown	400	Interferon	Exomphalos, right renal agenesis and hemivertebrae

OD indicates once daily; AFP, alpha fetoprotein; and NK, not known.

Molecular remission after imatinib discontinuation



Rousselot et al. Blood 2007 Jan 1;109(1):58-60

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