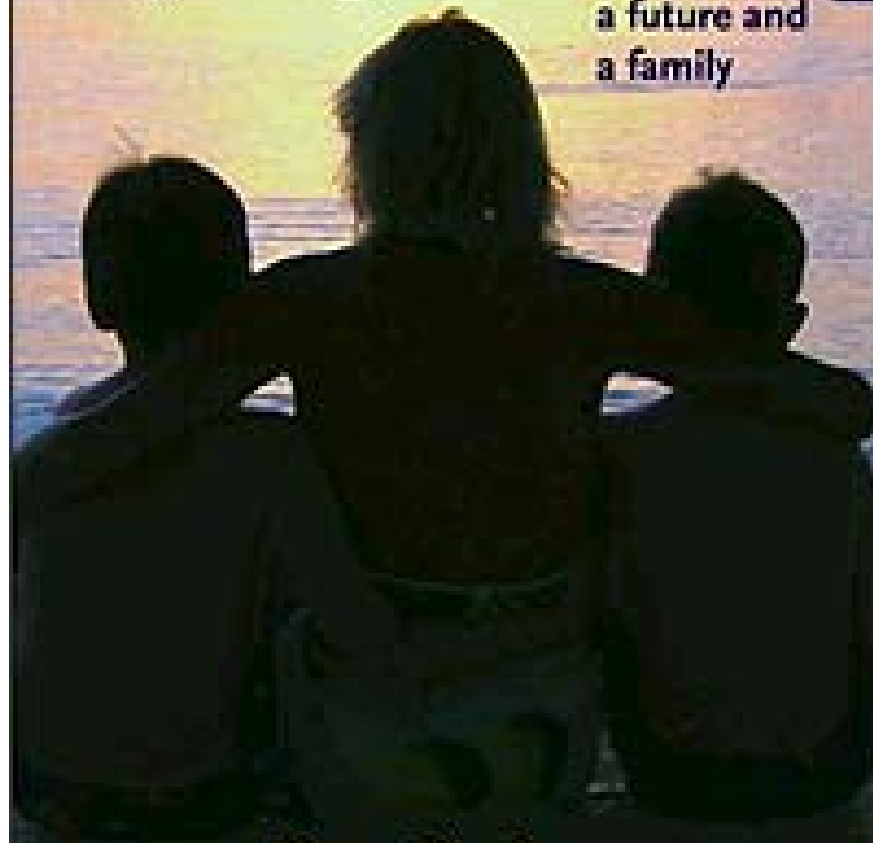


Chronic Myeloid Leukaemia Fertility & Pregnancy

Jane Apperley

Dying to Live

my fight for
a future and
a family



Fran Burke

with Helen Wilkinson

Case History 1

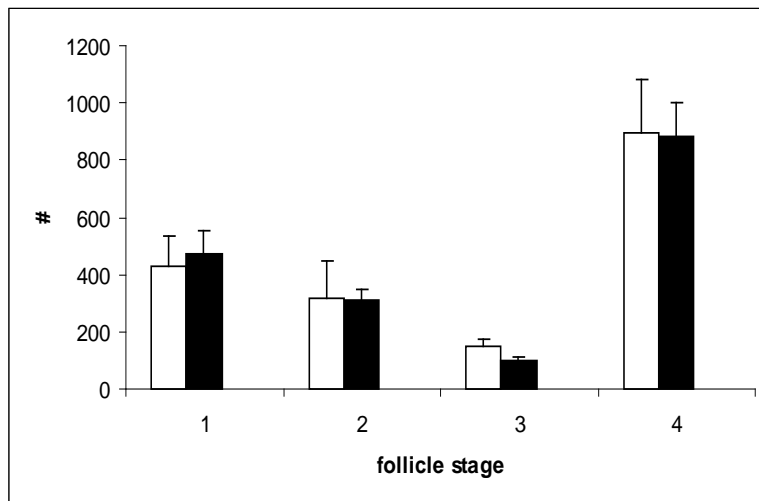
- Male patient aged 59, presented last week with profound fatigue and abdominal swelling
- Seen at major London hospital, diagnosis of CML in chronic phase made, prescribed imatinib
- Internet active wife: self-referred to me for consideration of EPIC (phase III randomised study of ponatinib vs imatinib)
- Unwell 6 months, fatigue attributed to birth of baby in Oct 2012
- 2nd marriage, first child by this marriage, 4th child of patient
- Should he enter study?

Management of fertility

- **Begins at diagnosis**
- **Consider immediate and future treatments**
- **If possible make provision for maintenance of fertility now**
- **Production of sperm begins 72 days before ejaculation, so chemo effects last at least 10 weeks after last dose**

Imatinib and fertility

Normal male and female mice fed with imatinib 150mg/kg per day for 12 months or placebo



□ *Normal water*
■ *Imatinib in water*

- No differences in follicular numbers and development
- No differences in spermatogenesis or size of seminiferous tubules
- No evidence for a direct effect of imatinib on fertility (ovarian & testicular function)

Imatinib, men and offspring

- Approximately 60 pregnancies reported in partners of men on imatinib
- No suggestion of any problems in conception, pregnancy, delivery or of any increase in congenital abnormalities

Pregnancy Outcome after 2G-TKI (men)	N=9
Normal Live Infant	8
Ongoing	1

Second case

- Female patient aged 37, pregnant with second child
- FBC at booking at 10 weeks, WBC $52 \times 10^9/L$
- Ph positive CML, Sokal score 0.7
- Patient wishes to continue with pregnancy

Pheresis in pregnancy

- Aim to keep WCC < 100 and platelets < 500
- Frequency varies between patients and at different times in the pregnancy: alternate days, weekly, fortnightly
- Frequency reduces in third trimester
- Does it work?

CML diagnosed in pregnancy

20 patients (2 miscarriages)

3 did not require treatment

1 received Hydroxyurea from week 16: normal delivery of a son at 36 weeks

14 managed by pheresis

- **14 live births**
- **13 normal, 1 with talipes**

Third Case

- **34 year old woman diagnosed with CML in June 2008, low Sokal score, no children**
- **Commenced on imatinib 400mg daily**
- **Complete cytogenetic response by 6 months, major molecular response by 12 months, most recent test (April 2010) RQ-PCR 0.004%**
- **She wants a family. What do we recommend?**

Imatinib in Pregnancy

180 pregnancies reported on imatinib

- We know the outcome of 125
- >70% received imatinib in first trimester only
- 26% received imatinib throughout pregnancy

Imatinib in Pregnancy

Pregnancy outcome	Total number	Percentage of those with known outcome (n=125)	Percentage 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 %

Fetal abnormalities (n=12)

Case 1: Premature closure of skull sutures

Case 2: Hypoplastic lungs, exomphalos (omphalocele), left duplex kidney, right absent kidney, hemivertebrae and right shoulder anomaly.

Case 3: Exomphalos, right renal agenesis and emivertebrae.

Case 4: Small exomphalos, scoliosis

The expected incidence of exomphalos in the general population is approximately 1 in 4,000

Advice for women who wish to become pregnant

Pre-conception	At least 24 months in MMR
Imatinib wash-out prior to conception	Not really necessary, perhaps stop at end of menstrual cycle
Disease monitoring	Frequency of RQ-PCR No treatment if remains in MMR/CMR Interferon in 2 nd trimester if RQ-PCR starts to rise
After delivery	Breast feeding contra-indicated

Advice will differ according to response

Complete/major molecular response

Complete cytogenetic response without MMR

**Complete hematologic response without
Complete cytogenetic response**

Advanced phase disease

Poor outcome after reintroduction of imatinib in patients who interrupt therapy for pregnancy without having achieved an optimal response

N	Sokal risk group	Months on imatinib prior to discontinuation	Clinical response at time of discontinuation	Clinical response at time of discontinuation according to ELN	Months without imatinib	Months of imatinib therapy after reintroduction	Clinical response after restarting imatinib
1	Low	9	MMR	optimal	9	30	CMR
2	Low	42	CCyR	suboptimal	9	18	No MCyR, subsequent loss of CHR
3	Low	21	CCyR	suboptimal	13	26	CCyR
4	Low	19	CCyR	suboptimal	23	29	no MCyR
5	Low	14	MMR	optimal	6	90	MMR
6	High	7	MCyR	suboptimal	8	50	MCyR
7	Low	50	MMR	optimal	13	14	MMR

What about 2nd generation TKI?

Pregnancy Outcome after 2G-TKI (women)	N=13*
Normal Live Infant	6*
Elective Termination	4
Spontaneous Abortion	2
Ongoing	1

** One pregnancy after nilotinib*

Imperial College London



Mary Alikian, Alex Bazeos, Marco Bua, Gordon Cook, Letizia Foroni, Gareth Gerrard, John Goldman, Ailsa Holroyd, David Marin, Dragana Milojkovic, George Nteliopoulos, Christos Paliompeis, Alistair Reid, Richard Szydlo, BSBMT teams and colleagues at Ariad, BMS, Novartis and Pfizer

**LEUKAEMIA
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Beating Blood Cancers

