



## The 65th ASH Annual Meeting Abstracts

## POSTER ABSTRACTS

## 632. CHRONIC MYELOID LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

**The Outcomes of Pregnancies in Japanese Patients with CML in the TKI Era; A Result of Nationwide Survey**

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**Background**

The introduction of tyrosine kinase inhibitors (TKIs) has dramatically improved the survival of patients with chronic myeloid leukemia (CML). Although the median age at diagnosis of CML is around 55 years, CML affects all generations, rendering a substantial population of women of childbearing potential. Therefore, issues related to conception and pregnancy are becoming increasingly important, because TKIs have the potential risk of fetal abnormalities and spontaneous abortion. Planned pregnancy during treatment-free remission (TFR) is an ideal way to avoid exposure of the embryo and fetus to a TKI. However, in real-life situations, not all conceptions are planned, not all patients fulfill the eligibility criteria for TFR, and some cases develop CML during pregnancy. Information about pregnancy in patients with CML is still limited in the TKI era.

**Study Design and Methods**

We designed a retrospective observational study of female patients with CML in the chronic phase who experienced pregnancy. We conducted a nationwide survey to collect data associated with CML treatment, conception, and pregnancy outcomes. This study was approved by the institutional review boards of Aiiiku Hospital and each hospital participating in the survey. This study is registered in the University Medical Information Network (UMIN000042762).

**Results**

We sent questionnaires to 463 hematological centers to ask whether they made a diagnosis of CML in female patients of childbearing age and we received replies from 206 centers (recovery rate: 44.5%). A total 853 female patients aged 45 years or younger were diagnosed as having CML between 2002 and 2020, and 78 patients became pregnant by December 2020. Information of 70 pregnancies in 49 patients was obtained for analysis. The median age at CML diagnosis was 26 (range, 9–40) years and the median age at pregnancy was 33 (range, 21–42) years. Times of pregnancy varied from once to five times, and times of childbirth ranged from zero to three times. There were three types of pregnancies: CML onset during pregnancy (n=9), unplanned pregnancy during treatment or stopping treatment with TKI (n=25), and planned pregnancy during TFR or treatment with interferon (IFN)- $\alpha$  (n=36). The median durations from CML diagnosis to first pregnancy were 4.1 years in patients with unplanned pregnancies and 9.1 years in patients with planned pregnancies. Nine pregnancies in patients with CML onset during pregnancy resulted in seven births and two elective abortions. Twenty-five unplanned pregnancies led to 14 births, eight elective abortions and three spontaneous abortions. In 36 planned pregnancies, there were 27 births, one stillbirth and seven spontaneous abortions, and one case was during pregnancy at the time of the search. Elective abortions were chosen in 10 pregnancies, possibly due to exposure of the embryo to a TKI (n=9) or due to not achieving MMR at the time of a positive pregnancy test (n=6). TFR was chosen in 31 pregnancies, resulting in 26 births and five spontaneous abortions. MMR or deeper response was sustained in 18 of 26 (69%) pregnancies with childbirth and 15 of 18 (83%) pregnancies with

DMR at the time of a positive pregnancy test. Treatment with IFN- $\alpha$  was chosen in 23 pregnancies and resulted in 20 births and three spontaneous abortions. Among the 13 patients with MMR or a deeper response at the time of pregnancy, only one patient (7.7%) lost MMR during pregnancy. Treatment with IFN- $\alpha$  was commenced after loss of MMR was experienced during pregnancy with TFR in four cases, with MMR being regained in two cases and CCyR being sustained in the other two cases until delivery.

### Conclusions

Although our analysis was based on a limited number of patients, TFR could be a reasonable option for patients who achieve DMR and desire childbearing. Treatment with IFN- $\alpha$  might be another option for pregnancy in patients who achieved MMR or a deeper response.

**Disclosures Kondo:** Pfizer: Honoraria, Speakers Bureau; Novartis: Honoraria, Speakers Bureau; Otsuka Pharmaceuticals: Honoraria, Speakers Bureau. **Matsuki:** Abbvie: Honoraria, Speakers Bureau; AstraZeneca: Honoraria, Speakers Bureau; Bristol-Myers Squibb: Honoraria, Speakers Bureau; Janssen: Honoraria, Speakers Bureau; Novartis: Consultancy, Honoraria, Speakers Bureau; Otsuka: Honoraria, Speakers Bureau; Pfizer: Consultancy, Honoraria, Speakers Bureau; Takeda: Honoraria, Speakers Bureau; Human Life Cord Sciences: Consultancy. **Takaku:** Novartis: Honoraria, Speakers Bureau. **Yoshida:** Abbvie: Honoraria; Bristol-Myers Squibb: Honoraria, Research Funding; Chugai: Honoraria; Janssen: Honoraria; Nippon Shinyaku: Honoraria; Novartis: Honoraria; Ono Pharmaceutical: Honoraria; Otsuka Pharmaceutical: Honoraria; Pfizer: Honoraria; Takeda Pharmaceutical: Honoraria. **Takahashi:** Novartis: Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; Asahi-Kasei: Research Funding; Pfizer: Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; Otsuka Pharmaceutical: Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; Astellas Pharma: Other: Commissioned research and joint research, Research Funding; Mochida Pharma: Research Funding. **Kimura:** OHARA Pharmaceutical Co., Ltd.: Honoraria, Patents & Royalties, Research Funding. **Matsumura:** Pfizer Japan Inc.: Honoraria, Research Funding; Janssen Pharmaceutical K.K.: Honoraria; ONO PHARMACEUTICAL CO., LTD.: Honoraria, Research Funding; Bristol-Myers Squibb Company: Honoraria; Genmab K.K.: Research Funding; Kyowa Kirin: Research Funding; Alexion Pharmaceuticals, Inc.: Research Funding; SymBio Pharmaceuticals: Honoraria; Novartis Japan: Honoraria, Research Funding; Otsuka Pharmaceutical Co., Ltd.: Honoraria; Eisai Co., Ltd.: Research Funding; TAIHO PHARMA: Research Funding; NIHON PHARMACEUTICAL CO.LTD.: Research Funding; SHIONOGI & CO., LTD.: Research Funding; Sumitomo Pharma Co., Ltd.: Research Funding; Asahi Kasei Pharma Corporation.: Research Funding; Takeda Pharmaceutical Company Limited: Research Funding; NIPPON SHINYAKU CO., LTD.: Research Funding; AbbVie GK.: Honoraria, Research Funding; AstraZeneca K.K.: Honoraria; Chugai Pharmaceutical Co., Ltd.: Research Funding.

Table 1

	Total	CML onset during pregnancy	Unplanned pregnancy	Planned pregnancy
Pregnant patients, n	49	9	24	24
Duration from diagnosis to the first pregnancy (yr), median (range)	49	not applicable	4.1 (0.8-14.2)	9.1 (4.2-16.1)
Total pregnancies, n	70	9	25	36
Age at CML diagnosis (yr), median (range)	26 (9-40)	28 (21-39)	24 (9-40)	26 (15-34)
Age at pregnancy (yr), median (range)	33 (21-42)	28 (21-39)	28 (21-39)	36 (27-42)
Treatment at the time of positive pregnancy test (n)				
none	10	9	1	0
TKI	23	0	23	0
IFN	16	0	0	16
TFR	20	0	1	20
Disease status at pregnancy, n				
without MMR	18	9	6	3
MMR/DMR	51	0	18	33
missing	1	0	1	0
Outcome of pregnancy				
spontaneous abortion	10	0	3	7
elective abortion	10	2	8	0
stillbirth	1	0	0	1
live birth	48	7	14	27
during pregnancy	1	0	0	1
Initial treatment during pregnancy				
none	6	5	1	0
IFN	17	2	2	13
TFR	26	0	11	15
Treatment at delivery				
none	4	3	1	0
TKI	4	2	1	1
IFN	20	2	2	16
TFR	21	0	10	11
Disease status at delivery				
without MMR	14	6	4	4
MMR/DMR	33	0	10	24
missing	7	1	0	0

Figure 1

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