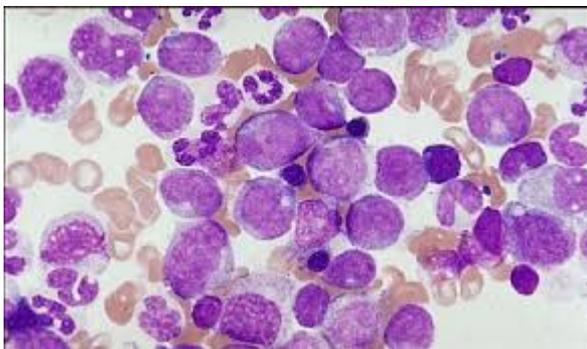


Fertility in Women Diagnosed with Chronic Myeloid Leukemia

Fertility in Women Diagnosed with Chronic Myeloid Leukemia

Women and men diagnosed with chronic myeloid leukemia should consider fertility issues and safety of pregnancy while under treatment. Chronic myeloid leukemia (CML) is formed of malignant cells from the bone marrow. It may later spread to the blood stream or other organs. It may also progress to a fast growing stage-acute leukemia. It is diagnosed in 2000 women and 2800 men yearly in The US, mostly during their adult years. Most individuals diagnosed with CML carry an abnormal chromosomal arrangement called Philadelphia chromosome. Many patients do not have any symptoms. CML is suspected from blood



counts and confirmed by examining blood smears and bone marrow examination.

Newer drugs like imatinib, dasatinib and nilotinib have changed the treatment of CML dramatically. More than 90% of patients that received these medications survived for 5 years or more. These belong to a group of medications called tyrosine kinase inhibitors (TKIs). These medication slow the propagation of lymphoma cells. Their side effects are less than standard chemotherapy. Response to treatment is assessed using blood counts, the presence of Philadelphia chromosome and molecular genetics tests for a specific gene. Some individuals require stem cell transplantation. Transplantation requires treatment with high dose chemotherapy and total body

irradiation, both are associated with very high risk for ovarian failure.

Effects of TKIs on fertility. *Animal studies* indicate that exposure to TKIs during adult life was not associated with impaired fertility in males and females. Exposure before puberty lead to reduced sperm production in males. There has been few case reports of low sperm count and early ovarian failure after exposure to imatinib in *humans*. This was not reported in large studies. Because of the possible effects of imatinib on fertility and because all individuals treated for CML are at risk for progressive disease requiring stem cell transplantation, men and women diagnosed with CML should consider fertility preservation. Men should consider sperm freezing. Women should consider embryo cryopreservation (if they have a partner) or egg freezing.

Effects of leukemia on pregnancy. In general pregnancy itself does not appear to affect the prognosis for leukemia There is no evidence that brief exposure to imatinib in early pregnancy is associated with adverse outcomes or abnormalities in the babies. There are no extensive data, however on the effects of imatinib and data on the effects of newer TKIs dasatinib and nilotinib are very sparse. Women are usually advised to use a birth control method while on these medications. In one study two of 16 babies had minor abnormalities (hypospadias in one baby and rotation of small intestine in one baby) that were surgically repaired. Women who were in remission and chose to stop imatinib during pregnancy, had 40 to 50% chance of showing evidence of propagation of the leukemia cells. The majority of them though achieved remission again after re-starting treatment.

Children born to men who are actively taking imatinib at the time of conception appear healthy and current advice is not to discontinue treatment. This is based on outcomes of 60 pregnancies reported worldwide in female partners of imatinib-treated men. In contrast the data relating to

children born to women exposed to imatinib during pregnancy are less encouraging. Although numbers are small-12 congenital anomalies were found among 125 pregnancies-there has been a cluster of rare congenital malformations such that imatinib cannot be safely recommended, particularly during the period of organ formation in the baby-first 8 to 12 weeks.

Women interested in getting pregnant while on imatinib and other TKIs should co-ordinate their specific care between oncologists and reproductive endocrinologist so that they attempt pregnancy while in remission for ideally 1-2 years and in the same time minimize the period of time while off treatment. Alternative treatments than TKIs can be used during pregnancy. After delivery, TKIs are restarted and breast-feeding is discouraged as the medicine is excreted in milk. Read more at <http://nycivf.org>